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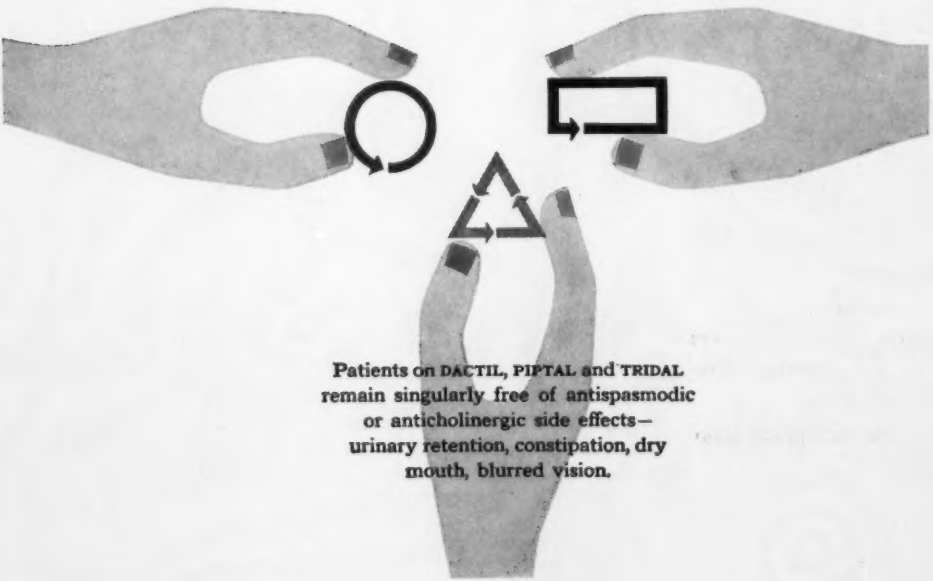

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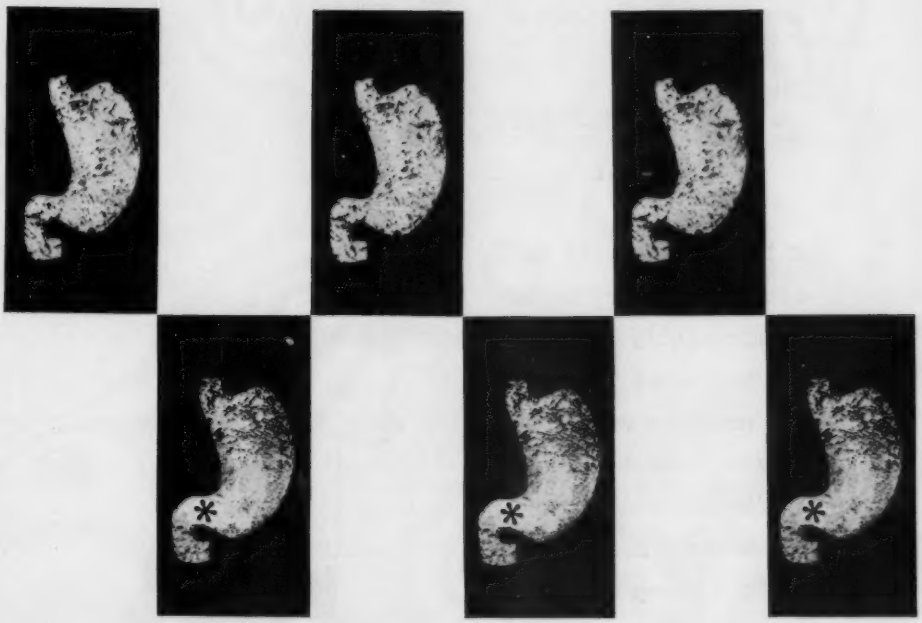

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The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

contents:

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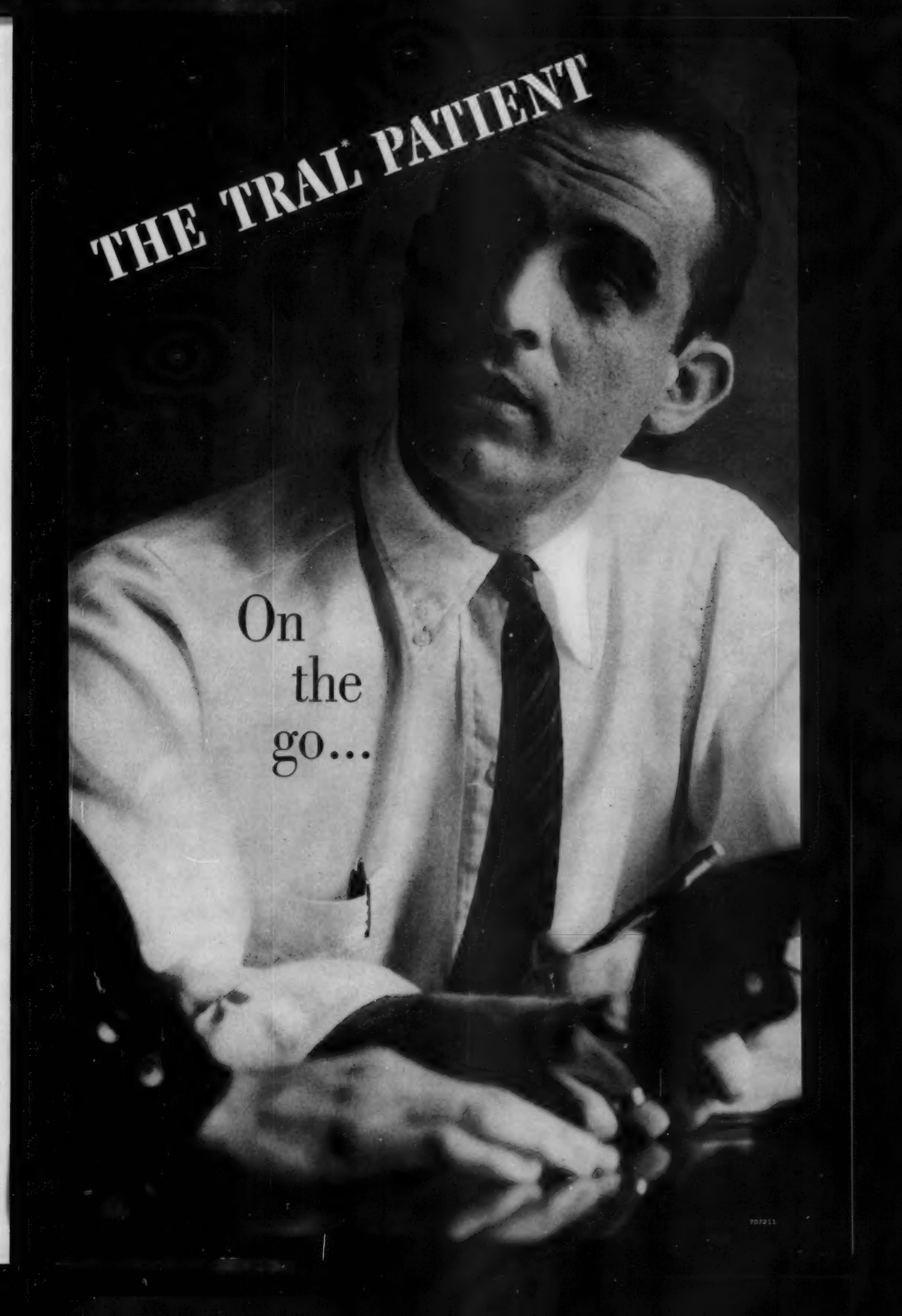
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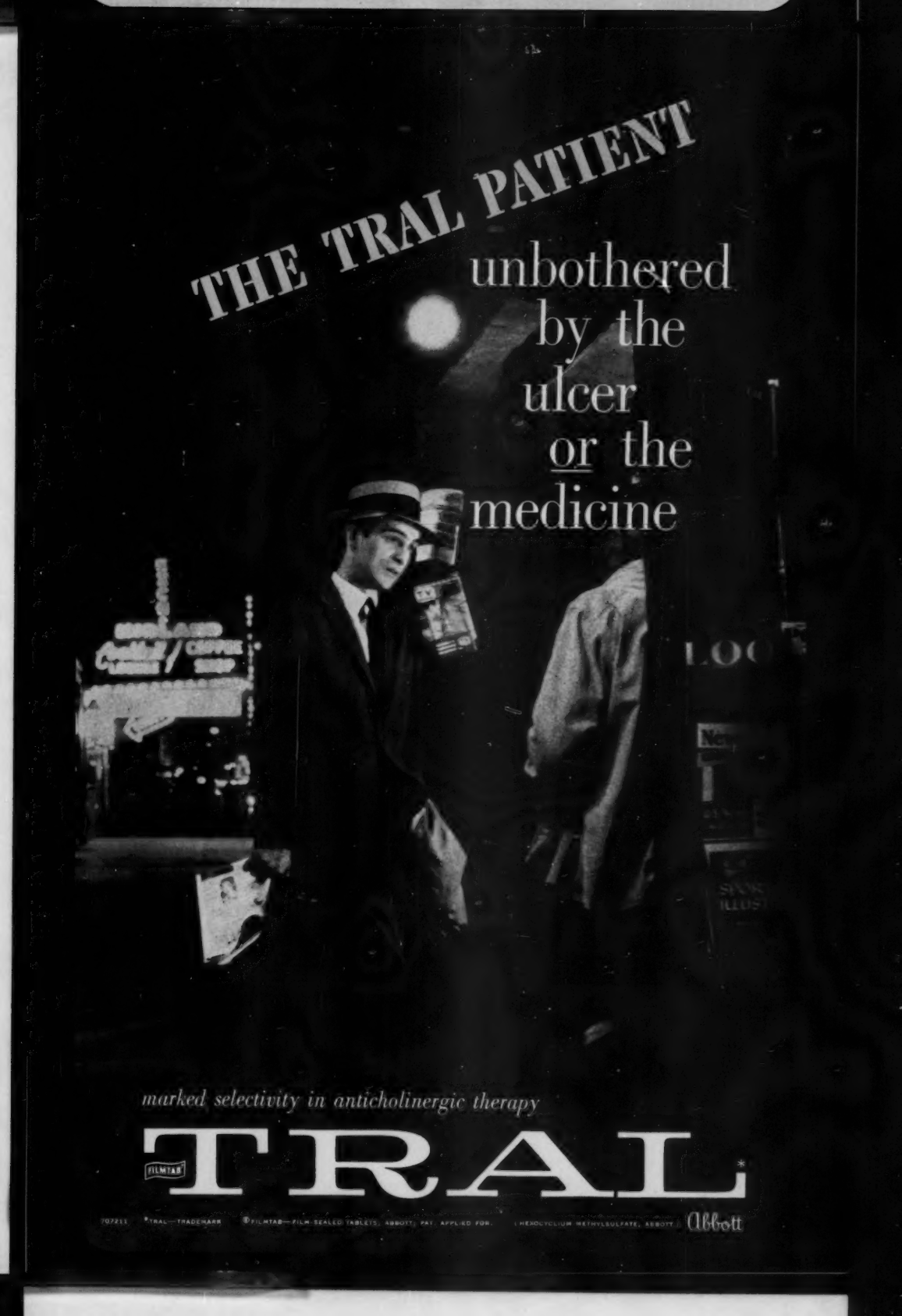
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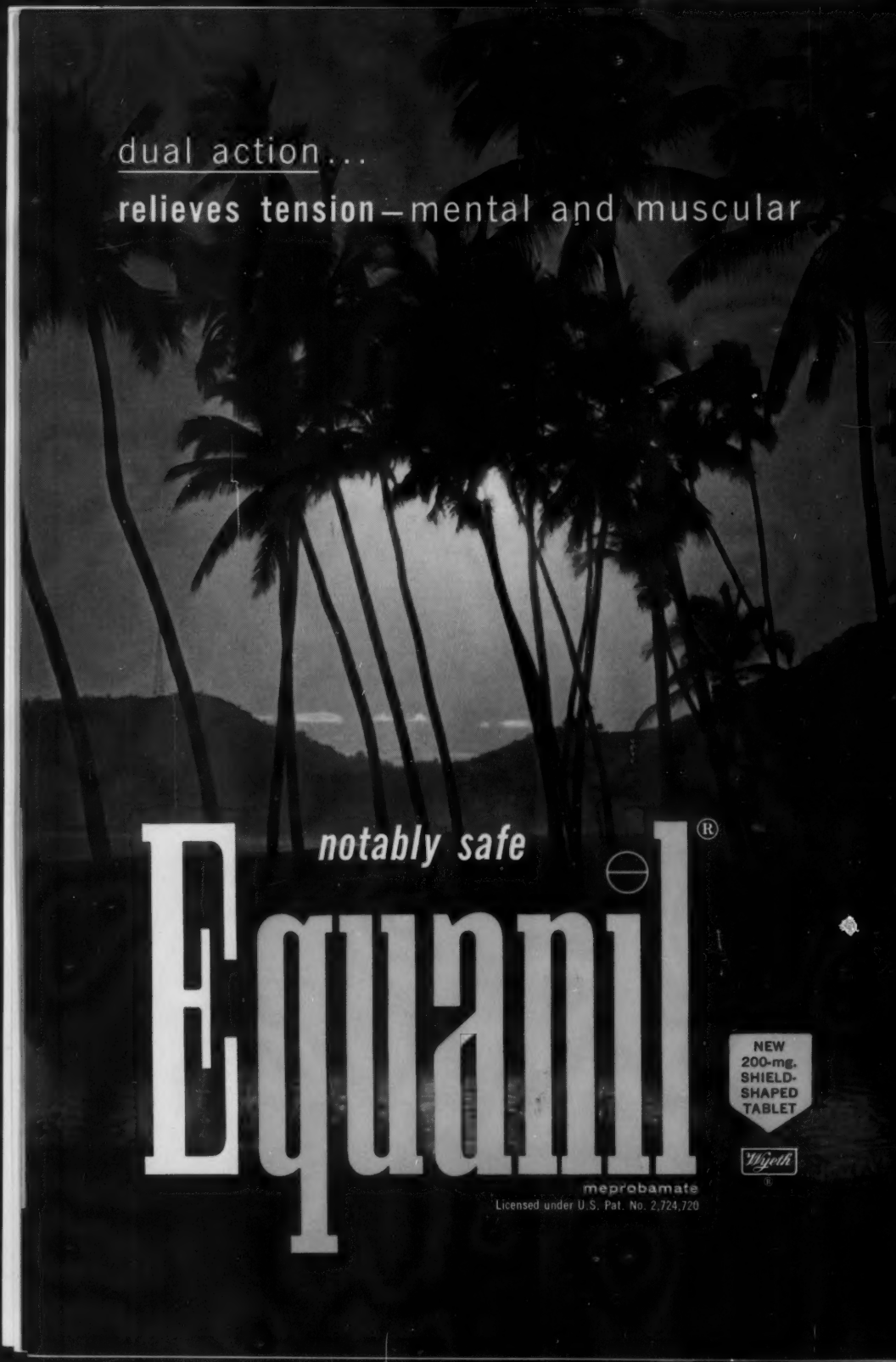
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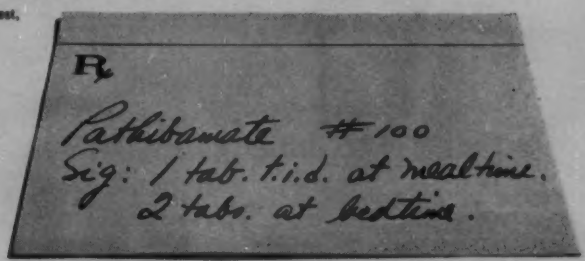

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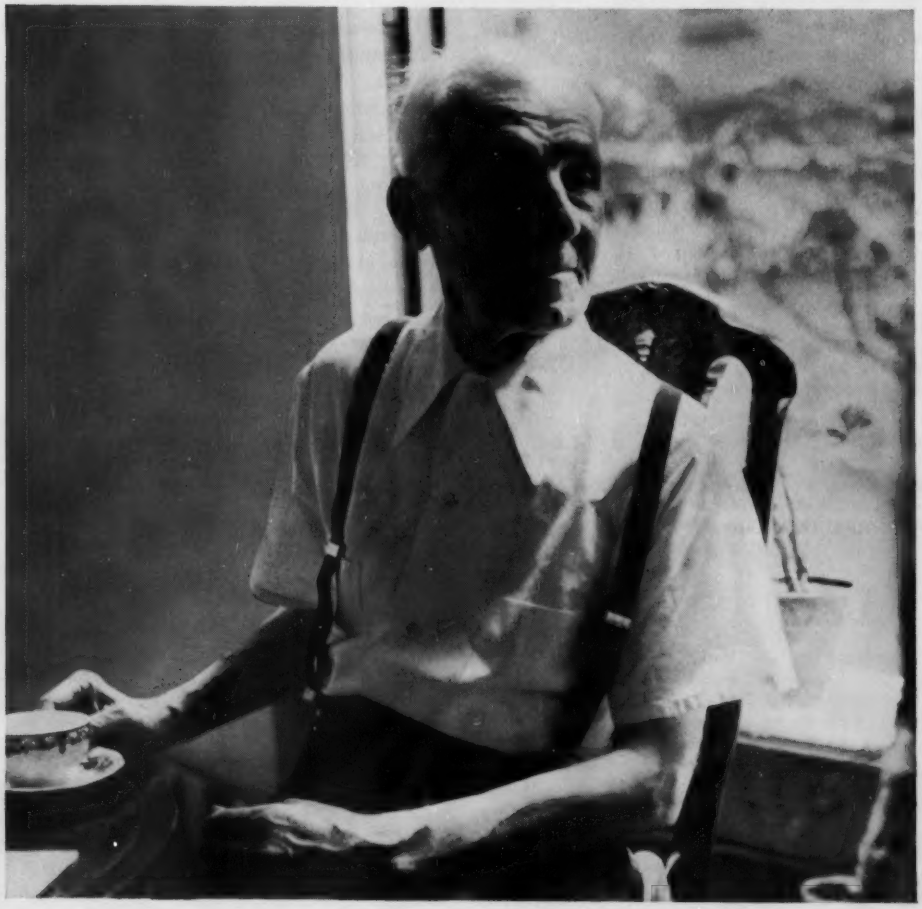

THE American Journal OF Gastroenterology

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VOLUME 28 AUGUST, 1957 NUMBER 2

PANEL DISCUSSION ON DISEASES OF THE SMALL INTESTINE*

MICHAEL J. LEPORE, B.S., M.S., M.D., *Moderator*†

THOMAS ALMY, A.B., M.D.‡

RICHARD H. MARSHAK, M.D.¶

RAFFAELE LATTES, M.D., D.Med. Sc.§

and

MILTON R. PORTER, M.D.**

New York, N. Y.

Dr. Michael J. Lepore:—It is indeed a privilege to be invited to assemble this group of distinguished people to discuss the problems of small bowel diseases. Originally when we were approached about this panel, we were asked to limit the participation to members of the staff of the Columbia University College of Physicians and Surgeons. We have adhered to this for most of our members. I have one outsider, a very distinguished one.

I am pleased to introduce Dr. Thomas Almy, at the end of the table, though he needs no introduction. He is Associate Professor of Medicine at Cornell University Medical College, and Visiting Physician and Director of the Second (Cornell) Medical Division, Bellevue Hospital.

In addition, one change has been made in the announced format of the panel. Dr. Louis A. Rottenberg requested that we obtain the help of Dr. Richard H. Marshak for this occasion. Dr. Marshak has done extensive study in this field, and Dr. Rottenberg felt he was better qualified to participate in this

*Presented before the Third Annual Convention of the American College of Gastroenterology, New York, N. Y., 15, 16, 17 October 1956.

†Assistant Clinical Professor of Medicine, College of Physicians and Surgeons, Columbia University.

‡Associate Professor of Medicine, Cornell University Medical College.

¶Associate Radiologist at The Mt. Sinai Hospital.

§Professor of Surgery, College of Physicians & Surgeons, Columbia University.

**Associate Professor of Clinical Surgery, College of Physicians and Surgeons, Columbia University.

panel. It was he who made the suggestion, and we are delighted to have Dr. Marshak, Associate Radiologist at The Mt. Sinai Hospital, present.

On my left is Dr. Raffaele Lattes, Professor of Surgery, College of Physicians and Surgeons, Columbia University, and Director of the Laboratory of Surgical Pathology, Columbia-Presbyterian Hospital Medical Center.

On my right is Dr. Milton Porter, Associate Professor of Clinical Surgery at the College of Physicians and Surgeons, Columbia University; Attending Surgeon, Presbyterian and Babies Hospitals; Visiting Surgeon, Francis Delafield Hospital, and Consulting Surgeon, Englewood and St. Albans Naval Hospitals. We are delighted to have Dr. Porter with us today.

Now, in orienting the discussion for this morning, I thought we might get a little start with a quotation that I happened to come across in a panel discussion in which Dr. Burrill B. Crohn participated, in 1954, on ileitis. He said, and this is a direct quotation: "I often like to muse about my days at the College of Physicians and Surgeons, when Dr. Evan Evans was Professor of Medicine. When we came to the chapter on the small intestine, Dr. Evans said, 'You can skip that chapter. There are no diseases of the small intestine, and, what is more, we know nothing about them.'" (Laughter)

I am sure Dr. Crohn will not mind if we dig back a little bit into the chronology of this statement. I found that Dr. Crohn was graduated from P. & S. in the class of 1907. This, then, would have been somewhere about 1905 or 1906, that Dr. Evan Evans made this statement, so that a good deal has happened since then, and if a good deal had not happened, there would be no justification for a panel discussion this morning before this audience.

It is to serve as a springboard for discussion this morning that I thought we would present some of the highlights of small bowel disease. We simply cannot cover the whole subject of small bowel disorders, but we will attempt to hit certain high points.

(Slide) The first slide is intended to emphasize what I call small bowel milestones, and they merely give us the perspective.

It was in 1895 that Roentgen made his gift to the world. In 1897 Dr. Cannon, a second-year medical student at Harvard, used bismuth suspension to study gastrointestinal motility. In 1928 Ross Golden did his first small intestine study. It was six months before anyone asked him to do another one.

In 1932 Dr. Crohn described what we now call Crohn's disease, or regional enteritis. In 1933 Dr. Wangensteen introduced his suction apparatus using the duodenal tube, and in 1934 the Miller-Abbott tube was introduced.

In 1933 and 1934, Dr. Tom Mackie noted changes in the small intestine in ulcerative colitis, and Snell and Camp, about the same time made some discoveries in sprue.

In 1935 came the development of vitamin therapy.

In 1946 the flame photometer gave us aid so we did not have to wait a week for a serum potassium report.

In 1951 anticholinergic drugs came into being.

In 1955 tagged isotopes–and who knows what next?

The following table presents in a panoramic view the disorders of the small intestine which occasioned this panel.

TABLE I

SMALL INTESTINE DISORDERS

Anatomical or Structural

- Resection of Small Intestine
- Short-Circuiting Operations
- Intestinal Fistulas
- Congenital Anomalies
- Volvulus
- Intussusception
- Meckel's Diverticulum
- Multiple Diverticula

Physiological or Metabolic

- Neurogenic
  - Parasympathotonia with Rapid Transit
  - Adynamic Ileus
  - Visceral Epilepsy
  - Diabetic Neuropathy
- Allergic
- Endocrinologic
- Hypoproteinemia
- Electrolyte Deficiencies
- Agammaglobulinemia
- Porphyria
- Plumbism

Pathological

Mesenteric

- Inflammatory
  - Sclerosing Mesenteritis
  - Mesenteric Lymphadenitis
    - Tuberculous
    - Nontuberculous
- Neoplastic
  - Hodgkin's Disease
  - Lymphoblastoma
  - Metastatic Carcinoma
  - Mesenteric Cysts

Intestinal

- Inflammatory
  - Regional Enteritis
  - Primary or Secondary Amyloidosis

Sarcoidosis
Scleroderma
Strictures of Small Intestine
Multiple Adhesions
Simple Ulcer
Bacillary Dysentery
Parasitic Diseases
Giardiasis, Amebiasis, Ascariasis, Uncinariasis,
Strongyloidiasis, Schistosomiasis
Fungus Diseases
Blastomycosis, Histoplasmosis, Moniliasis
Whipple's Intestinal Lipodystrophy
Lipidoses-Gaucher's, Nieman Pick's, Xanthomatosis
Pneumatosis Cystoides Intestinalis

Vascular

Periartheritis, Systemic Lupus
Erythematosus, Thrombotic Thrombocytopenic Purpura,
Arteriosclerosis, Mesenteric Thrombosis

Neoplastic

Benign
Fibroma
Myoma
Lipoma
Adenoma
Endometrioma
Hemangioma
Lymphangioma
Polyposis (Peutz-Jeghers Syndrome)

Malignant

Infiltrating Type
Fungated or Polypoid Type
Intramural
Extramural
Carcinoma; Primary or Metastatic
Primary Lymphosarcoma
Plasmacytoma
Metastasizing Carcinoid
(Serotonin Syndrome)
Leiomyosarcoma
Periepithelioma

Primary Malabsorptive or Nutritional Disorders

Celiac Disease
Tropical Sprue
Nontropical Sprue
Gluten Sensitivity
Kwashiorkor
Vitamin B-Complex Deficiency Disorders

Now, this illustrates some of the problems, and I think we have come a long ways since the statement of Dr. Evan Evans in 1905. With this as an introduction, we can ask the members of our panel to open the discussion of these diseases.

We thought we would start in this way: I should like first to have some discussion of the methods for studying small bowel disease, the role of the various people of the team that approaches the study of the patient with small bowel disease, or suspected small bowel disease, and I should like to have Dr. Thomas Almy initiate the discussion of the role of the internist in the diagnosis of small bowel disorders.

Dr. Thomas Almy:—The internist is usually thought of as the man who brings in a large array of diagnostic measures to pin down the diagnosis, but often he happens to be the first person to suspect that the seat of the disorder of the patient is in the small bowel.

I should, therefore, like to emphasize one symptom and one sign which I think are much neglected. First is the location of the pain in small bowel disorders. As you know, there is both clinical and experimental evidence showing that the pain from the mesenteric small intestine is most likely to be referred to the periumbilical area; yet this simple fact is widely neglected. Second is that the diarrheas are often to be identified as to their locus of origin on the basis of the size of the stool. I am sure you are familiar with the frequency with which a very large stool is passed by patients with small bowel disorders.

As to the methods of study, I think we should say that we can study at least three basic functions of the small intestine today by means readily applicable to man, motility, absorption, and the function of the argentaffin cells.

The methods for the study of motility, other than radiologic, which Dr. Marshak will comment on, are not commonly used for clinical purposes; yet we have a bewildering array. We now go far beyond the old rubber balloon with electromanometric pressure recordings, strain guages, and a variety of other technics, in all of which the records end up on a multiple channel electrocardiograph apparatus.

Further, in the last year or two we have learned that the motility of the small bowel may be measured to some extent by the sound it produces. This may seem like a highly qualitative and subjective sort of thing; yet the sound engineers are able to analyze the harmonic values of sounds produced and recorded. It is quite possible that at some time in the future this may provide a quantitative objective method for the study of small bowel function.

The methods for the study of absorption, I think, are of the greatest importance in the whole area, from the point of view of the internist. I shall merely try to emphasize certain principles in their use, and those that I think are the most desirable. The most convenient, of course, are those methods which relate to the increase in the blood level of a substance after it is absorbed from the intestine.

There is the oral glucose tolerance test. This can be improved upon by using other sugars, such as galactose and xylose, in which the level in the blood

stream is more critically related to the rate of absorption. One can go farther to study the rate of absorption of methionine or Vitamin A, or use the butter tolerance test, in which the serum turbidity increases to a certain degree after the absorption of butter or some comparable fat. But all these methods only indicate the *rate* of absorption of these agents from the intestine. They do not indicate the *total efficiency* of the absorptive process, and for methods of this kind we have to depend upon the *disappearance* of the ingested substances from the intestinal contents. This can be measured in one of two ways, by the quantitative chemical measurement of the substance in the stool, and subtraction of this value from the intake, or by the disappearance from the intestine of an isotopically labeled substance, usually fat.

It seems on the basis of recent studies from several laboratories, that we will soon have a workable method, and a thoroughly reliable method, for absorption measurements through the use of fat isotopically labeled with I^{131}.

I think it is wise to reflect on the variability of stool output from day to day. Those who have run metabolism wards will generally agree that to get accurate measurements of the content of the stools for various substances, such as fat and minerals, it is necessary to pool the output into long periods of time. I think that we should require at least three-day collections of stools for the purpose of study of absorption.

Also I think we should remember how inefficient and unreliable is the collection of any excreta on ordinary hospital wards. This can be checked easily when one is attempting to collect 24-hour urine, and we know that the collection of urine is often unreliable and incomplete. We have a less satisfactory check for the stools, and we must remember that this is an important source of error in a fundamentally simple method of study.

I finally would like to mention only the fact that the presence of excessive numbers of functioning argentaffin cells, as in a large carcinoid tumor, is now measurable by the metabolic end-product of the serotonin produced by these tumors. The test for 5-HIAA in the urine is certainly a new and interesting development and a help in the discovery of very unusual lesions of the small bowel.

Dr. Lepore:—Thank you, Dr. Almy. We will now call on Dr. Richard Marshak to discuss the role of the radiologist in the diagnosis of the small bowel diseases, or disorders.

Dr. Richard A. Marshak:—Many methods are utilized for examination of the small intestine. Time does not permit an analysis of all of these. I should like to present the method we have found most successful in elucidating some of the problems concerned in small intestinal diseases. The small intestine is studied following the administration of a mixture containing 10 oz. of barium sulfate by volume to which has been added enough water to make 20 fluid

ounces. We use ordinary commercial USP barium sulfate. The initial film is made at 15 minutes and another after a 15-minute interval. Further filming depends on the rate of passage of the barium meal and usually consists of an examination every 30 to 60 minutes. Neither saline nor ice water are administered because these preparations in themselves, in our experience, disturb the small intestinal pattern. In the interpretation of diffuse lesions of the small intestine, large quantities of barium should be used, so that many intestinal loops may be visualized in continuity at the same time. In sprue, for example, the loops of bowel may be so dilated that small amounts of barium administered may pool in a single segment. Small amounts of barium may not reflect the

Fig. 1a Fig. 1b

Fig. 1a–Moderate dilatation of the mid and distal jejunum. The loops are pliable and undulating. There is no evidence of any rigidity.
Fig. 1b–Marked dilatation of the mid and distal jejunal loops.

morbid anatomy of the small intestine due to incomplete filling and frequently the incomplete distention may simulate an abnormality. Ardran, French and Mucklow have stated that with the use of their micropulverized barium preparation, segmentation which is so frequently seen in malabsorptive states can be prevented and a continuous barium column produced. This is advantageous in recognizing the organic structure of the small intestine. It may have the disadvantage, however, if used on the initial examination, of obscuring the functional changes which may aid in the diagnosis of malabsorption states.

I would like to briefly review some of the criteria used in diagnosing small intestinal lesions, specifically, sprue. Dilatation of the lumen of the small intestine is one of the most important and constant findings (Figs. 1a and 1b).

Some of the individual features of the sprue pattern are seen in other disorders, but in none is dilatation more striking or constant than that associated with sprue. It is usually best visualized in the distal jejunum. The dilated loops are generally long, tortuous in course with pliable walls. The *valvulae conniventes* are prominent. Dilatation appears to be related to the severity of the disease and is most marked in the advanced cases. The large intestine may also show dilatation which can be pronounced. The cause of dilatation is unknown. It may be related to the thinning of the bowel wall, excessive secretions, potassium deficiency or possibly an autonomic nervous system imbalance.

The second common finding is segmentation (Figs. 2a and 2b). This is usually most pronounced in the ileum and best seen in the more advanced cases. Two forms are noted, immediate and delayed. The more common form is delayed segmentation (Fig. 2a), namely, segmentation that occurs in those intes-

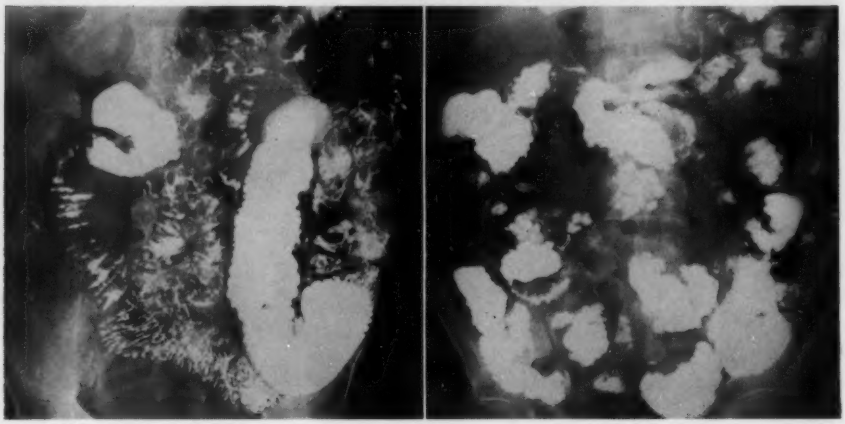

Fig. 2a

Fig. 2b

Fig. 2a—Marked segmentation, fragmentation, increased secretions. The segmentation in this case is delayed.

Fig. 2b—Immediate segmentation. The segmented loops are large and separated from one another. Moulage sign and increased secretions.

tinal segments that are in the process of evacuation. Immediate segmentation (Fig. 2b) is noted as soon as the barium enters the small intestine and persists throughout the study. The term segmentation in our reports has been restricted to indicate only those clumps of barium which are large, definitely separated from adjacent clumps, usually dilated and containing excessive secretions. The small contracted barium-filled segments of small intestine connected by strands of barium seen in association with spasm are not included in this definition.

An excessive amount of secretion in the intestinal tract is a constant phenomenon in most cases showing the sprue pattern and especially in those with marked segmentation.

When dilatation of the jejunum occurs, whether due to mechanical or functional changes, the mucosal folds, rather than becoming flattened, are prominent and seemingly enlarged. In sprue, the *valvulae conniventes* in the dilated jejunum can appear remarkably conspicuous (Figs. 1a and 1b). This is in contrast to the usual autopsy findings of a smooth atrophic mucosa. The dynamic state of the bowel is not reflected in the postmortem findings and it would appear that prominent mucosal folds produced by an active muscularis mucosa are lost. The thickening of the folds seen in lymphosarcoma and Whipple's disease is more readily understood. The actual infiltration of mucosal and submucosal layers of the bowel wall produce thickening, stiffening and rigidity of the infiltrated area with accompanying reactive edema.

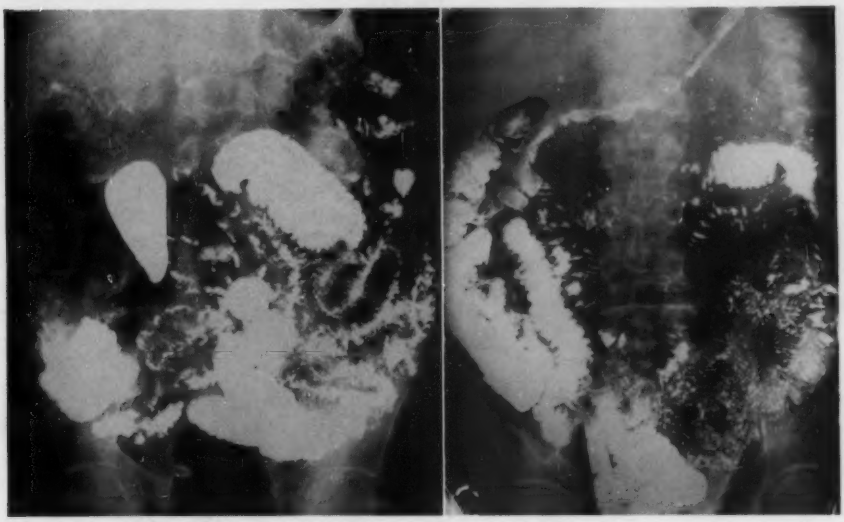

Fig. 3a Fig. 3b

Fig. 3a–Segmentation, collapsed loops of bowel, increased secretions and moulage sign.
Fig. 3b–Minimal segmentation, fragmentation, increased secretions and a patient with toxic capitetus.

The term "moulage sign" (Figs. 2b and 3a) has been utilized to describe the roentgen appearance of the jejunum in sprue, in which the folds appear to be completely effaced and the barium-filled lumen resembles a tube into which wax has been poured and allowed to harden. It is most frequently noted in association with hypersecretion and segmentation. When the changes of dilatation, segmentation, hypersecretion are noted as described above, we use the term "sprue pattern" rather than the nondescript terms "deficiency pattern" or "disordered motor function". The mechanism of production of functional changes in the small intestine has been little understood and all variations in

the appearance of the small bowel which were considered functional were grouped under the term deficiency pattern. The inclusion of so many disorders often because of the presence of one roentgen variation has caused such a dilution of the term "deficiency disorder" that it has lost its meaning. It has been recognized for many years that deficiency no longer is the basic factor responsible for the changes. The continued use of this term has prevented the recognition of specific patterns within this all-inclusive group. The studies made in our patients suggest that the roentgen appearance, when characteristic, is usually associated with marked steatorrhea and it is suggested that the term "sprue pattern" be utilized for these severe functional alterations. The sprue pattern may also be seen with a slightly less intensity in secondary steatorrhea, such as Whipple's disease and lymphosarcoma.

I would like to describe briefly some of the roentgen features in regional enteritis.

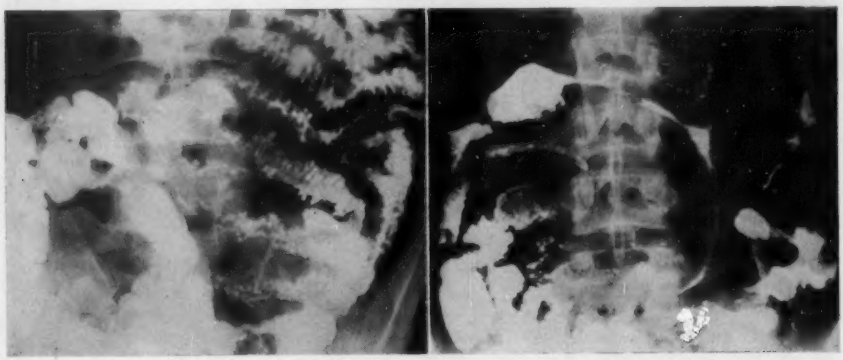

Fig. 4a Fig. 4b

Fig. 4a—The folds are thickened, blunted and in some cases fused. The contour is irregular. There is rigidity and separation of the loops of intestine. Both intestinal loops appear straightened or uncoiled. Diagnosis: Nonstenotic type of regional enteritis.
Fig. 4b—Long rigid narrow segments resembling pipestems with marked separation of the loops of bowel. Diagnosis: Stenotic phase of regional enteritis.

Several investigators have divided the roentgen findings in this disease into acute, subacute and chronic stages. Since the classical form of regional enteritis is that of a low grade inflammatory process with episodes of acute exacerbation, it is difficult to identify such a clear-cut pattern. Acute granulomatous regional enteritis has been described, but the determination of the precise time of onset of this disease is unusually difficult. What is described as acute regional enteritis may be the more active phase of this chronic illness.

Proximal and distal extension of the disease process, despite repeated roentgen examinations extending over a period of many years, was not observed.

The maximum length of involvement was determined on the initial roentgen studies. This is not true after exclusion operations when recurrent disease is frequent.

One of the prominent features of this disease is the development of stenosis with obstruction. Therefore, roentgenologically, the cases may be divided arbitrarily into stenotic and non-stenotic groups. It is impossible to classify these groups as early and late, since the majority of cases may continue without stenosis for many years. Again, division into active and inactive seems inappropriate, as the patient with long segments of stenotic bowel may also exhibit considerable evidence of clinical activity, manifested by fever, diarrhea and abdominal pain.

The earliest mucosal alterations are blunting, flattening and thickening of the *valvulae conniventes* (Fig. 4a). The folds are arranged in a fairly regular

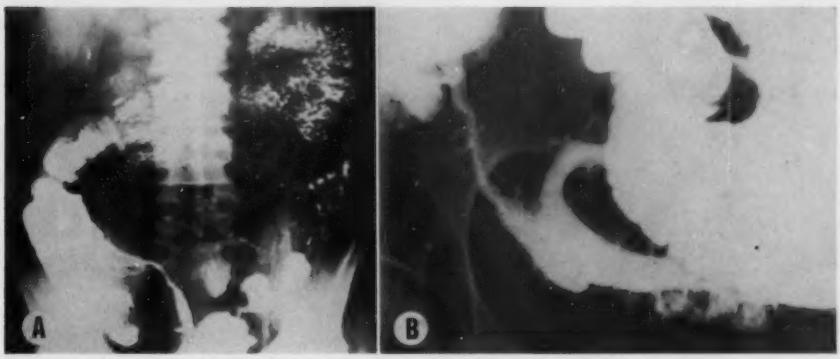

Fig. 5a Fig. 5b

Fig. 5a—Marked narrowing and irregularity of the terminal ileum with a fistula to the sigmoid. Diagnosis: Terminal ileitis with a fistula to the sigmoid.
Fig. 5b—Terminal ileitis with numerous sinuses and fistulas. Some of these extended into the urinary bladder.

symmetrical parallel fashion and as progression occurs, may become thicker, irregular and partially fused. The bowel lumen becomes irregular in width. These changes are due to the inflammatory submucosal and mucosal thickening. When ulceration occurs a more characteristic pattern is produced. Longitudinal streaks of barium recognizable as ulcerations appear. As the thick, blunted folds of mucosa are further destroyed, cobblestoning may be noted. Ulceration continues at the expense of the intervening islands of mucosa, replacing the cobblestone pattern by an irregular network of interlacing streaks of barium. The appearance at this stage has no uniformity or symmetry and is hazy and reticulated. Denudation of the mucosa is usually incomplete, leaving behind islands of inflamed mucosa which produce multiple smooth defects of varying size.

Their prominence is increased by the narrowing of the bowel lumen which is due to beginning cicatricial contraction that occurs at this stage. Finally, one may see the radiologic image of a uniform, rigid, castlike tube filled with barium and presenting no mucous membrane pattern. This is similar to ulcerative colitis and represents the stage when scarring and regeneration of an atrophic mucosa is progressing. As scarring proceeds, the transition to the stenotic phase occurs (Fig. 4b). Carcinomatous transformation of these polyps has not been observed. Coincident with changes in the mucosa, other characteristic roentgen features occur. The bowel lumen reveals varying degrees of narrowing. Early, the submucosal thickening and associated spasm are responsible for the narrowing of the lumen. Later, as fibrosis occurs, the narrowing is more marked. In the early stages, rigidity of the contour and mucosal pattern is incomplete. Some flexibility or dynamic activity is evident in the change in contour and mucosal pattern during successive roentgenograms. Later, the roentgen appearance is fixed and unvarying. Pliability is lost. Also early in this disease, the normal serpentine or coiled pattern of the loops of small bowel disappears. The diseased segments appear to be straightened and rigid. This finding is probably due to loss of flexibility of the bowel wall and mesentery as well as longitudinal shortening due to spasm.

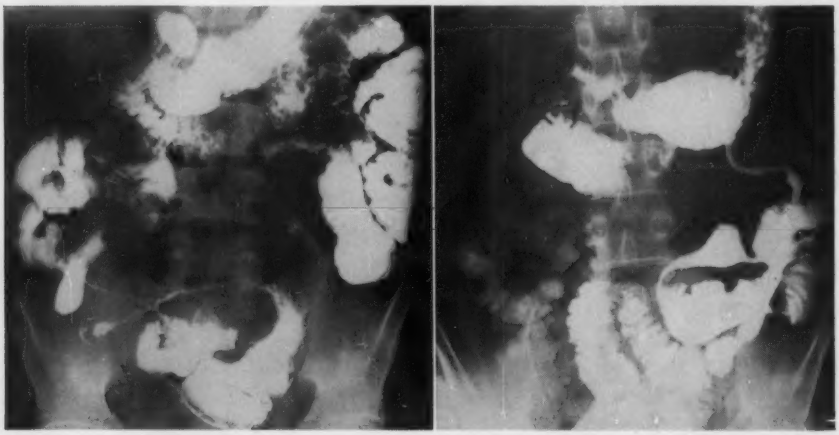

Fig. 6a

Fig. 6b

Fig. 6a—The distal jejunum and proximal two-thirds of ileum show long areas of narrowing alternating with areas of dilatation. The mucosal pattern in the stenotic areas is reticulated. The loops of intestine are widely separated and rigid. Diagnosis: Stenotic phase of ileojejunitis.

Fig. 6b—Constricted segments starting at ligament of Treitz alternating with areas of dilatation in jejunum. There is considerable dilatation of the duodenum. The mucosal pattern in constricted areas appears cast-like. Diagnosis: Stenosing jejunitis.

Frequently, the loops of intestine appear to surround a mass (Fig. 4b). Although this may be due to an abscess resulting from perforation, more often it is secondary to the indurated mesentery, associated with the marked increase in the mesenteric fat and the enlarged lymph nodes.

In the stenotic stage, many of the rigid loops described previously become constricted to a remarkable degree (Fig. 4a). These stenotic segments resemble rigid pipestems. This appearance is due to a marked thickening and contraction of the wall of the small intestine. The stenosis may extend through 1 or 2 cm. or over long segments. With severe narrowing, dilatation of the proximal intestine may be marked.

The most frequent site of involvement of the small bowel with regional enteritis is the terminal ileum. Five hundred and six cases revealed involvement of the distal 9 to 12 inches of terminal ileum. One hundred and twenty-six patients had involvement of the entire ileum.

The string sign which has come to be identified as the pathognomonic roentgen manifestation of regional enteritis is most frequently noted in this region. It has been described as a thin, linear shadow, suggesting a frayed cotton-string in appearance. The cause of the string sign is incomplete filling due to irritability and spasm associated with marked ulceration and may be seen in both the nonstenotic and stenotic phase of this disease. Repeated spot films will demonstrate the fact that some distensibility is still present in this segment. The bowel proximal to the string sign may or may not be dilated depending on the stage of the disease. In the nonstenotic phase the proximal intestinal lumen is generally not dilated despite the marked narrowing associated with the string sign, indicating the importance of spasm in producing this characteristic appearance. This spasm is usually inconsistent. When persistent, temporary proximal dilatation can occur with symptoms of obstruction. In the stenotic phase there is constant proximal dilatation which may be accentuated by spasm secondary to ulceration. Despite the narrowing complete intestinal obstruction is rare. The recognition of the fact that the string sign does not always indicate marked fibrosis and stenosis is important as exclusion operations during the stage of marked ulceration and activity have been followed by a high degree of recurrence. Because of the marked ulceration, fistulas and perforation (Figs. 5a and 5b), thickening of the mesentery and separation of the loops of bowel are more frequent in the distal ileum than in the remainder of the small bowel. A possible explanation of the marked ulceration in the distal ileum may be the higher bacterial content in this area. Any portion of the small bowel can be involved with regional enteritis. It is less common in the jejunum (Fig. 6b) and duodenum. Cases involving the stomach have also been reported. Regional enteritis usually stops abruptly at the ileocecal valve. Extension into the colon, however, can occur.

Following sidetracking operations for regional enteritis, recurrent disease in the new terminal ileum is not infrequent. Recurrent disease is most frequent during the first year. Many years may elapse, however, before recurrence takes place. Recurrences also appear to be more frequent in those patients where the initial lesion reveals marked ulceration with fistula formation.

In the cases where operation is performed because of stenosis, the recurrence rate appears to be less. The length of the lesion has no effect on the recurrence rate. In general, the recurrent lesion acts similarly to the original process. The colon is rarely invaded and the usual site is the new terminal ileum.

Dr. Lepore:—Thank you, Dr. Marshak. Those were very pretty illustrations of these various lesions.

I think it is only fair to point out that there may be some controversy about the use of 24 oz. of barium for the study of the small intestine. In Dr. Golden's studies he recommends 4 oz. of barium in normal saline. This controversy of flocculable and nonflocculable barium is interesting. In some institutions flocculable barium has not been accepted, and there must be differences of opinion in many quarters regarding the usefulness of these substances.

Now, for the next phase of the program I have asked Dr. Lattes to discuss the role of the pathologist in the study of small bowel disorders. This, I think, will give us some orientation as to the quantitative aspects, what to expect statistically in a series of patients with small bowel disease. Dr. Lattes!

Dr. Raffaele Lattes:—I believe that the role of the pathologist, in the handling of diseases of the small intestine is generally no different from the role of the pathologist helping the clinician in the study and diagnosis of other disease conditions.

I should like to start by making a plea and a warning: You will get the best results in accuracy of diagnosis if your pathologist is a "member of the team" rather than an isolated specialist, working in a separate pavilion of your medical center, to whom you send small fragments of tissue, with little or no information, but with the request for a precise diagnosis.

We feel that the pathologist is another consultant specialist, like your consultants in other fields, and in all diagnostic problems we want to be thoroughly informed regarding the clinical picture and pertinent findings in the patient prior to exploration or biopsy, or definitive operation. For instance, we want to be in the operating room at the time of the surgical procedure so as to inspect *in situ* what might be found by the surgeon, and to discuss with the surgeon the significance of the findings and possibly the site and type of biopsy to be taken.

I learned this lesson from my teacher, Dr. A. P. Stout, and now I expect our resident surgical pathologists, when they are in charge of the frozen section

service, to be familiar with the clinical and the operative findings, and not render an histological report unless they are thoroughly informed of the condition of the patient as a whole.

(Slide) I prepared a slide last week which is a breakdown of the relative frequency of the diseases, mostly in the surgical domain, of the small intestines as we see them in the department of surgical pathology of the Columbia-Presbyterian Medical Center.

You can see right away that the most important single condition in our material was the so-called regional enteritis, or Crohn's disease, of which we had 137 cases. It is possible that this figure is slightly inflated in the sense that probably at least a dozen of these represent repeated operations on the same patients. On the other hand, these figures include only the cases that came to operation.

The problem of regional enteritis will be discussed later on.

Among the important surgical conditions of the small intestine, the next in order of frequency was a surprise to me. It seems that the most frequent tumors of the small intestine are the primary carcinomas, at least in our material. Even after you take out the 30 duodenal cases of carcinomas, you have 34 primary carcinomas against 26 lymphosarcomas, and 21 carcinoids of the small intestine, so that while we agree that the primary malignant tumors of the small intestine are rare, and adenocarcinoma is rare, it is not the rarest one.

What is the role of the pathologist in this respect? It is, again, to collaborate with the surgeon at the time of operation in confirming or ruling out the clinical diagnosis. We have great accuracy with the frozen section method, taking biopsies either from the primary tumor mass or from possibly involved regional lymph nodes. I believe this method of the frozen section is perhaps the more important in that it helps in identifying the histologic type of the tumor. We all know that different tumor types that are considered malignant have a different natural history and therefore different therapeutic procedures are indicated. Certainly in some instances it is better not to embark on any radical procedure such as for example, when there is extensive involvement by a lymphosarcoma.

There is no further time to discuss this point, but if there will be questions from the floor I shall try to answer them.

Recently we have had occasion and opportunity to collaborate with internists, gastroenterologists, and surgeons, in studying and identifying at operation, diseases belonging to the so-called malabsorption syndrome.

(Slide) This is a section from a mesenteric lymph node, from a patient, a man who had a so-called malabsorption syndrome, with loss of weight, fatty stools, blood in the stools, and low Vitamin A in the serum, and so on. The

internist suggested the possibility of the rare disease known as Whipple's intestinal dystrophy. At operation a large lymph node was removed and this lymph node was a large, yellowish, obviously lipoid mass.

(Slide) This is a photomicrograph of the lymph node, in which you can see a cribriform pattern, and the holes are vacuoles of fat surrounded by phagocytic cells.

(Slide) This fat stain shows that they contained lipid.

(Slide) And this stain is the so-called Periodic Acid Schiff reaction, in which it is shown that in the section you saw before there was also strongly PAS positive material which is generally thought to be a glycoprotein. These findings are not 100 per cent diagnostic of the disease, but, together with all the other data and laboratory findings, it was possible to make a diagnosis in this case which, if I am not mistaken, was one of the first cases diagnosed in life. We have recently had occasion to study pathologically other rare manifestations of malabsorption syndrome.

(Slide) This is a case studied by my associate, Dr. Lane, in cooperation with the clinicians, in a patient with loss of weight and symptoms of small intestine malabsorption disorder. At operation, the surgeon found that the wall of the small intestine was intensely pigmented in brown color.

(Slide) This shows, side by side, two fragments of this intensely brown, pigmented intestine, and another section from another nonpigmented case. This case, studied very thoroughly by the histochemists with all the known histochemical methods, proved that the pigmentation was due to the presence of a rare lipochrome, which in experimental animals has been shown to be frequently associated with deficiency of Vitamin E absorption. I don't know whether we will ever again see a case of that sort, but now that we have learned the significance of that finding, I believe if we see it again, we will be guided in the right direction in this rare disorder.

Dr. Lepore:—Thank you very much. I am sure that Dr. Lattes meant that that was the first case of Whipple's disease that was diagnosed in a living patient at the Columbia-Presbyterian Medical Center. There have been others. At the time of this discovery there had been at least five others, four or five, several of them at Duke University, on Dr. Julian Ruffin's service down there.

Now we turn to the man in the fourth place in our batting order, the clean-up man, who has the role of the surgeon. We, as internists, have evidenced some reluctance to turn any of this material over to the surgeon in the past. We thought that by the use of our tagged isotopes, and x-ray studies, and other things, we could make a diagnosis, but we know very well that we simply cannot make the diagnosis in a number of these patients, and it is in these well-studied cases that we turn for help to our colleague on the surgical service.

Dr. Porter has been very active in this regard, with us, and he has been through a number of very trying situations with us. I hope he will tell us something about these. Dr. Porter!

Dr. Milton Porter:—Thank you, Dr. Lepore. Perhaps the most trying situation of all is to stand looking at such bowel. You have just seen a picture of it and perhaps you are wondering what we did next. We didn't do a thing in that case. I might give you the build-up. This was a 62-year old mechanic who for eight years had intermittent pain and watery diarrhea, which, when worked-up, proved to be sprue. He had fat in his stool. He had had an inguinal hernia done in another hospital, and ascites was discovered. At the time when we had him, he did not have ascites. His gastrointestinal series revealed a diaphragmatic hernia which was known for years, but the upper jejunum was dilated to the extent of 5 cm. with prominent mucosal folds and, to top it off, the psychiatrist called him psychoneurotic.

In the operating room the small intestine was boggy and dilated, and his lymph nodes grossly enlarged. His entire bowel was tan in color, and it was worse in the jejunum. He has since operation (at which time biopsies were the only thing done) been kept on Meticorten. At the last visit, the dose was doubled because he seemed to have a relapse, some ten months after the operation. He had shown improvement in the ten months up to the last visit.

Our job as surgeons is to explore people and explore them knowledgeably. We have to work up the cases with people like Dr. Lepore and the roentgenologists to know what is suspected and to understand the differential problem. The small intestine is a terribly hard place for anyone to find a lesion. The radiologists are awfully good, but they miss a lot of things, and so do we, even though we may finger through the entire gastrointestinal tract from end to end.

Dr. Golden, who probably has done as many small intestinal series as anyone, told us before he left our institution that he had only diagnosed one or two Meckel's diverticula anteoperatively in his career.

I should like to point out another clinical trick. I don't know whether this was Dr. Golden's idea originally, but certainly it has pulled the fat out of the fire a number of times—if I may be permitted to talk about diagnostic things and not just treatment. He had the habit, in certain confusing cases where the small intestinal series was done in the usual way and had failed to reveal the presence of a lesion which everyone really felt must be there, of putting a Miller-Abbott tube down the terminal ileum and irrigating barium through the Miller-Abbott tube, in this way avoiding the overlying proximal loops of intestine, which sometimes would mask a lesion in the terminal ileum.

I have in mind one case where, having been missed on two previous small intestinal series, a carcinoid of the terminal ileum was found. Putting down the Miller-Abbott tube has been a good thing, in the cryptogenic bleeder cases.

Especially, in cases who have been worked-up in the usual way and who come in again with recurrent hemorrhage. The chap who sees them first takes a Miller-Abbott tube and pops it down and finds the most proximal level at which blood is present in the gastrointestinal tract. This may be helpful knowledge to the surgeon coming up empty-handed after exploration. It is nice to know how high up the blood has been detected. The intestine then can be opened and, with a sterile sigmoidoscope at laparotomy, bleeding angiomata and other impalpable lesions may be picked up.

We do, in our explorations of the gastrointestinal tract, when the going is tough and we can't find what we are looking for, resort frequently to the use of the sigmoidoscope in the operating room. If one puts it in the antrum of the stomach, one can examine from the esophageal hiatus down to and around through the entire duodenum and even upper jejunum. We open the intestinal tract at other levels to look over suspicious areas with the 'scope.

Most of the cases we diagnose, we diagnose because we are led to explore because of hemorrhage, obstruction, or signs of peritonitis. There are, however, certain diseases which are not, strictly speaking, small bowel diseases, which have the ability to masquerade as small bowel diseases. These come particularly to my mind because of the relative frequency with which we, as surgeons, are called upon to treat them.

The mesenteries may be infiltrated with carcinoma. These people may present as cases that seem to be mechanical obstruction and may be almost indistinguishable from them. When explored, they are found to have nothing the matter with the small intestine, but a cancer-riddled mesentery interrupting transmission of nervous impulses through the bowel's autonomic nervous system.

We have had cases of appendicitis which have mimicked diseases of the small bowel. One individual was referred to me for appendectomy, but I convinced myself that this young man of 23, with recurrent right lower quadrant and periumbilical pain, fitted the picture of regional ileitis and I did not explore him immediately. I referred him to Dr. Golden. Dr. Golden told me that on x-ray examination, the films showed classical regional enteritis. I therefore prescribed a medical regime, and with the help of his medical doctor, he was carried along for a period of a year, during which time he had a mild flare-up approximately every six to eight weeks.

At the end of the year he came in one day with what was classical appendicitis, and we decided there was no reason why a chap with regional enteritis couldn't also get appendicitis. It was too hot to sit on so we operated and we found he had an appendix at least as long as a pencil, and intimately adherent to the distal ileum. Every time it heated up it gave the x-ray picture of regional enteritis in that part of the ileum. An appendectomy solved his problem. I was a little too cautious and outsmarted myself in this instance.

There is another type of case which we are being called upon to explore with increasing frequency, and properly so. This is a good illustration of it: A 66-year old businessman came in. In the past he had had a gastric and duodenal ulcer documented, mild diabetes, which began in 1954, benign hypertrophy of the prostate and arteriosclerotic heart disease. He came in with five weeks of nonbloody loose stools (five or so a day), mild epigastric distress, and some weight loss. The work-up showed stool guaiacs 1 or 2 plus, fat in his stool, a small bowel, motor physiology that was disturbed, a normal bilirubin, and an alkaline phosphatase which was up a little bit, but recently he had had chlorpromazine, which can put that up without putting up the bilirubin. His duodenal content showed almost no trypsin at all. His fasting blood sugar was 143, and serum carotene level was zero.

Dr. Lepore and I thought this was evidence that he was not putting out adequate pancreatic juice, and that, everything coupled together, it was prudent to find out what it was that had shut off the pancreatic duct. We explored him, and found we were right diagnostically but could not do a thing to help him. He had carcinoma occupying almost all of the pancreas except the areas in which it would have to be to cause jaundice.

This led us into exploring carcinoma of the pancreas we otherwise might have waited on for some time. We have had other experiences like this. These cases with the lipochromatosis case, illustrate how the surgeon is correctly called upon to explore for sprue.

I think the other things I have to say, Dr. Lepore, can probably be said when you come to enteritis.

Dr. Lepore:—Thank you very much, Dr. Porter.

I think we can go on to some specific disorders of the small intestine, or perhaps we should say nonspecific disorders. We thought we would start the discussion of sprue or the malabsorption syndrome, and for this I will call on Dr. Almy again.

Dr. Almy:—Thank you, Dr. Lepore. I will try to concentrate on recent changes in our understanding of this condition.

I feel that in the last few years there has been the gradual formation of a composite picture of the fat absorption mechanism which most people will accept, and I have attempted to summarize this on one slide. (Slide) You know there have been two main thoughts regarding the mechanism of fat absorption: first, the indication at the bottom of the slide, that there is complete hydrolysis of the dietary fat to fatty acid and glycerol, these being absorbed through the intestinal mucosa as such; and, the other thought, that there is particulate absorption of emulsified fat, indicated in the upper half of the diagram, and that these particles go unchanged through the intestine.

At the present time most students of this subject consider that both mechanisms exist, but that the bulk of the fat we take in, particularly that containing highly saturated and long chain fatty acids, is only partially degraded by pancreatic lipase to mono- or diglycerides, and pass through the mucosal cell, along with completely undegraded fat particles.

This involves the formation of an emulsion which consists of undegraded fat, the mono- and diglycerides, and some free fatty acids; these go through the lymph vessels to the thoracic duct, and finally are dumped in the blood stream. The fats containing short chain and unsaturated fatty acids are mainly split by lipase in the presence of bile, are then absorbed through the intestinal mucosa, are carried to the liver and there metabolized partly to neutral fats which are characteristic of the organism itself.

These two pathways, I think, have some significance not only in their relationship to the problems of fat absorption in sprue but also in our understanding of the fate of certain dietary fats in relation to atherosclerosis.

The next subject that I think is worth mentioning is a growing awareness that secondary sprue, or symptomatic sprue—in which malabsorption is symptomatic of an organic disease of the small intestine—is not only a very common phenomenon in the experience of large modern medical centers, but also a disease condition which is very difficult to differentiate from the idiopathic sprue.

We have seen in our own experience approximately 20 per cent of patients with the sprue syndrome to be associated with lymphosarcoma. We were unable to make a differentiation from idiopathic sprue until the disease had progressed to such an extent as to perforate the intestine, or to involve other parts of the body with lymphosarcoma, which is a fairly late phenomenon.

Thirdly, I should like to emphasize the two steps that have been made in recent years in the better treatment of the syndrome of idiopathic sprue. I am sure you have all read a great deal about steroid therapy, and possibly most of you have used it. I thought you might be interested in some pictures of the first case that we treated with ACTH, in 1950, and I should like to use these to show you the magnitude of the changes which have been seen when such therapy has been used.

(Slide) This is the appearance of this patient at the time that ACTH therapy was started. She weighed 29 kilograms, with an original body weight of 65. In six weeks she had had an increase of 15 kilos in her weight, with subsidence of all the signs and symptoms of sprue.

(Slide) This shows the increase in body substance. What is a reasonable and proper duration of steroid therapy in sprue? It seems to us that this therapy should be continued until the normal body weight has been restored or an

acceptable plateau is reached and maintained for a period of three or four months, before an attempt is made to terminate the chronic administration of minimal amounts of steroid. We have ourselves preferred to do this extremely slowly, rather than to taper it abruptly and then terminate it with a course of ACTH.

This patient was treated with steroids of various kinds for more than three years, and was then tapered-off over a period of six months. She has since remained asymptomatic on no therapy for nearly three years, with a body weight in excess of her original body weight.

The other measure that I am sure is of interest at the present time is the gluten-free diet. You know, this was originally developed in the therapy of celiac disease in children, in Holland, in Denmark, and in England, and has been broadly applied to adults and patients with sprue. We seem to have had as good luck as anybody with this in adult patients. We feel that this is probably because of the excellent dietitians that we have at the New York Hospital, because in comparing notes on specific elements of the dietary plan with gluten-free diets established elsewhere, we find that our dietitians have been able to find gluten in many foods and food products which have not been suspected elsewhere.

A patient whom I saw yesterday was sent from a major medical center in another city, and this patient was eating rye bread, Rye-Krisp, and corn muffins made out of regular corn muffin mix. All of these substances contain large quantities of gluten. I think the expected efficiency in this dietary plan will come only with the exclusion of gluten in fairly complete fashion.

(Slide) Here is a clinical summary of the first six patients we treated with this condition, after having really worked on the diet; you will see that all of them have had a remission of symptoms, all of them with complete relief from diarrhea. All of them have gained weight, and the remission has lasted for from 8 to 36 months, on no other form of therapy.

We emphasize that the patients controlled on this diet can eat any amount of fat and roughage, and need no other alteration in their dietary plan.

(Slide) Here are some studies on one patient. You will note that the glucose tolerance test, which was pretty normal at the beginning, did not change. The weight increases. The serum albumin rises during therapy. The prothrombin level, which had been greatly reduced before the diet was started, returned to normal without supplementary Vitamin K, and the calcium level rose without large supplements of calcium or Vitamin D.

(Slide) Here is a balance study of fat and nitrogen in four separate periods. The black portions indicate the content of these substances in the stool. The figures in these columns indicate the percentage of fat absorbed in each period.

The shaded area here is the urinary nitrogen. You will see that in the first ten days of the use of the gluten-free diet there was only a slight increase in fat absorption, and not up to the normal level.

A few months later, when the patient was returned, after gaining considerable weight, the fat absorption was essentially normal.

There may be some improvement in the diarrhea in the first day or two, but it is not often striking, and it takes six to eight weeks before one can sense the full advantage of the diet for the patient.

(Slide) Here are changes in the small intestine by x-ray—before therapy on the left, and on the right—during therapy with the gluten-free diet.

I strongly suspect we are going to find people who, despite all reasonable care in the use of this diet, are not getting a good clinical result. We know this has happened in other institutions, and I think we have just been lucky; nevertheless, at the present time we would feel that the average patient with sprue, in a nonemergent situation, deserves to have a trial on the gluten-free diet before any other general program of management is required, except the repair of specific deficiencies, such as B_{12} deficiency, or hypocalcemia.

We feel that because of the slow onset of the maximum benefit from this therapy, it either should be preceded by or combined with the use of steroids in patients who are acutely ill when they are first seen, because the action of these agents is considerably more rapid.

Dr. Lepore:—Thank you, Dr. Almy. We are running a little short of time, and we are going to have to make some changes in the original format of our panel discussion.

For the next phase of it, it is unfortunate that I do not have a copy of *Life Magazine* or *Time Magazine* for discussion of the disease which is of international interest. We are going to turn to Crohn's disease of regional ileitis, and I wonder if Dr. Almy would initiate that discussion, too.

Dr. Almy:—I feel the only thing I can say here which would be worthwhile, just to throw out the ball, is to remind you of the chronicity of this disease and of certain facts about its nature which influence our activities as clinicians. We all feel very humble about this because we have known about it for such a relatively short period of time, and it is obvious that our therapy and our attitude toward it have to be judged by the effects obtained over many, many years.

Our own feeling is that this phenomenon, presenting in effect a chronic granulomatous process, with no evidence of an invasive, communicable microorganism, is something which deserves to be treated like tuberculosis, except that we can be much more free and much more hopeful in the use of the steroids in its management.

I am sure there are many more specific points you would like to get to.

Dr. Lepore:—Yes. We have some questions, and I hope we can get to those, if we leave a few minutes for questions and answers at the end of the panel.

I wonder, Dr. Porter, if you would say something about the surgical measures in the management of regional enteritis.

Dr. Porter:—The mere presence of the disease does not mean an operation is indicated, as Dr. Almy has just pointed out. If, however, under adequate medical treatment the patient continues to lose too much weight and is severely anemic, or if the complications arise of obstruction, hemorrhage (which is admittedly rare), perforation, abscess, or fistula formation of the type that is a serious problem to the patient—and not all of them are—then operation may be indicated.

We see the disease in two phases. First as acute ileitis, sometimes found by the surgeon when he is looking for an acute appendix,—and there are cases of acute ileitis which cannot be told clinically from acute appendicitis. In a good hospital the thing to do is look and be certain which disease you are dealing with. Assuming there is no obstruction or perforation and the patient has typical ileitis with nothing in his history suggestive of long-standing disease, we teach our residents and practice ourselves the business of closing the abdomen without doing anything to the ileum.

The question always arises in these discussions whether or not to take out the appendix, and I don't think anyone on this platform can make a statement about whether or not that is to be done in an individual case. It comes down to this: if the cecum, from which the appendix hangs, is normal, and the place in which one puts his purse-string suture is essentially normal, then we would take the appendix out. If the inflammatory process is so close to the point of origin of the appendix, or if the cecum itself is the site of a primary inflammatory process, we would prefer to leave the appendix rather than trust working with such tissues.

If the person were obstructed at the time, and we went in thinking it was intestinal obstruction and not appendicitis, we might elect to do one of the other procedures which I will mention in a minute as I talk about the chronic type.

The abdomen is closed with or without removal of the appendix—and I might say that practicing selective removal of the appendix depending upon the circumstances present, will, I think, keep fistula formation to a minimum. We have had none that I can remember offhand, when these rules have been carefully followed. Silk purse-string sutures are almost invariably used in the cecal wall when we do our appendectomies. The person then goes down to

the ward, where he is treated with antibiotics and steroid, and so on, much as Dr. Almy has outlined.

The second clinical form in which we meet the disease is the chronic type. The disease has been known to exist for some time and the person becomes obstructed, or develops fistulas, or abscesses. These people are explored, and there are certain individuals whose disease process may have produced an abscess, and whose disease is so extensive as to defy doing anything at that time other than draining the abscess.

This is not the usual situation. We feel that if it is possible to do it, without accepting an untoward risk in the estimate of the surgeon, it is better to remove the involved ileum than to leave it. It is not necessary to remove it, but, if one can bring normal bowel ends together, with the anticipation of no trouble at the time of anastomosis, it appeals to us as a good method of treating the disease. The matter of whether you can take it out is not a very simple one to speak about, because the terminal ileum may be glued to the right ureter or be so close as to make you worry about trying to mobilize it, and the mesentery may be so extremely thick as to almost defy management. In these instances, we embark upon the business of short-circuiting the diseased area.

There are various ways of doing this, that have been talked about. I am sure you are all familiar with it. I have put two of the commonly mentioned ones on the blackboard. The one on your right side is one which we would prefer to limit to those individuals where speed is of the essence, for some reason. (Simple side-to-side ileotransverse colostomy in continuity).

But in general we would rather do the one on the left (Division of the ileum with end-to-end ileotransverse colostomy, and leaving blind loop of distal ileum in the abdomen). One danger exists if you leave the abdomen, having derailed the fecal stream into the transverse colon. The diseased blind limb can, in certain instances, be obstructed at its midpoint and blow out the stump, or form a large cystic mass. In a few instances I have brought it out to the skin as a functionless fistula, which safeguards against this.

Dr. Lepore:—How about resection?

Dr. Porter:—I have already mentioned that we resect unless it cannot be done with safety. If there is a big, edematous mass, with things like the ureter dangerously near it, we leave it, having steered the stream out of the loop. This does not guarantee that fistulas cannot be formed from the diseased loop, even though it has been defunctionalized, but the incidence of this must be low.

Our experience has not been large enough to make us feel that we can speak about these things with great conviction, but this is the way the wind is blowing in our hospital at the moment.

It is interesting to note that we have one case of this disease limited to the duodenum. It occupied a large part of the duodenum. Fortunately, this does not happen often and, of course, if it is in the duodenum, one does not blithely remove it, because it requires a tremendous operation.

Dr. Lepore:–Dr. Porter, we have some questions and they are quite interesting. Here is a question Dr. Nix asks:

Is the congested, thickened appendix, occasionally seen at time of emergency appendectomy, an early acute phase of regional enteritis? If so, what per cent progress to chronic regional enteritis?

Dr. Porter:–We have one case identified as typical acute appendicitis, reported as acute appendicitis, by the laboratory, and the man has returned with enteritis, which we have treated by ileocolectomy. Review of the appendix shows it had granulomatous lesions in it. Presumably it was the same disease for which we have just operated. It happens occasionally.

Dr. Lepore:–A question from Dr. Cane: Is there histological evidence to support the opinion that regional enteritis is a manifestation of collagen disease of "rheumatic" nature?

Dr. Lattes:–That seems to be a loaded question. I would say that to those of us with a morphological point of view, regional enteritis is a granulomatous inflammatory lesion. I am in agreement with Dr. Marshak that it is probably not preceded by a nongranulomatous condition. I have never seen a section, or a gross specimen, of regional enteritis in which there wasn't a granulomatous process. If I have seen them, I know that I have not diagnosed them as regional enteritis.

As far as the term "collagen disease" goes, I think it is a term that has perhaps been misused, or at least used quite loosely. I don't believe there is any proof that the disease is of a rheumatic nature.

It is interesting that one-half of regional enteritis cases when studied will show histological areas in which there are tubercle-like granulomata. I don't believe anyone has ever demonstrated the presence of tubercle bacilli by culture or otherwise. We have never been able to discover them by bacterial stains in tissue sections and so far as I know there is no proven case that ended up in systemic sarcoidosis. We can only register the fact that in about one-half of the cases of regional enteritis there are sarcoid-like or tubercle-like granulomatas whose nature we are unable to define.

I would answer the question in this way: We have no morphological evidence that there is any connection between rheumatic disease and regional enteritis.

Dr. Lepore:–There is one question here which we are not going to ask anybody to answer, but it might be of interest to read it:

"Given a 66-year old individual, whose daily life is filled with tensions and responsibilities, and who has already had an ileocolic anastomosis for regional ileitis, what chance would you say he would have for a relapse of his disease in the next four years?"

I think we will file that one. (Laughter)

Dr. Lepore:—Dr. Lattes, you brought out this material from the laboratory on the incidence of these various diseases, and this question reads:

"Slide on the incidence of small intestinal diseases shows regional enteritis 130 cases, Meckel's diverticulum 90 cases, and carcinoma 60 cases. Do you really find carcinoma one-half as often as regional enteritis?"

TABLE I

SURGICAL PATHOLOGY OF SMALL INTESTINE
1928-1956

Most important lesions of small intestine, in order of frequency, from the files of the Surgical Pathology Laboratory, Columbia University, College of Physicians and Surgeons

Regional Enteritis:	137 cases	Lymphosarcoma of All Types:	26 cases
Meckel's Diverticulum:	95 cases	Carcinoid:	21 cases
Diverticulum of Other Types:	72 cases	duodenum:	4 cases
(including 53 duodenal diverticula)		jejunum:	2 cases
Carcinoma:	64 cases	ileum (and ileocecal valve):	14 cases
duodenum:	30 cases	Adenomatous Polyp:	17 cases
jejunum:	20 cases	Leiomyoma:	11 cases
ileum:	14 cases	Leiomyosarcoma:	8 cases
Heterotopic Pancreas:	48 cases	(1 of Meckel's diverticulum)	
duodenum:	39 cases	Enterocystoma:	4 cases
jejunum:	6 cases	Endometriosis:	2 cases
terminal ileum:	1 case	Whipple's Disease:	1 case
Meckel's diverticulum:	2 cases	Metastatic Tumors:	rare

Dr. Lattes:—In that group of cases I think the answer is yes. You have to remember that the material that was listed represents surgical pathological material from the surgical service of a general hospital. We have to say we have had about one-half as many carcinomas, including those of the duodenum, as cases of regional enteritis that came to operation.

Dr. Lepore:—Here is a question for Dr. Almy: Dr. Wirts would like you to comment on the advantages and limitations of I^{131} labeled fat absorption test.

Dr. Almy:—I must confess to having had no personal experience with this, only knowing about that of my neighbors and friends. There has been a lively discussion over some years as to whether the iodine tag would stay on the fat during the passage through the bowel; whether it might not be separated off and be absorbed in the blood stream, giving a falsely high impression of the

degree of absorption of fat. I believe there is now general agreement that this is not a problem, that the bond of the iodine is stable, and that the measurement in this respect will be a reliable one.

I feel that as soon as we have gotten a little more data from various sources indicating what is the true range of normal in this test, we can look forward to substituting it for the chemical measurement of fat in the stool in the laboratories that are equipped to do it.

Dr. Lepore:—Dr. Marshak, here is a question for you:

"Discuss the relationship of x-ray findings and the clinical picture in sprue."

That is a good question. Perhaps some of the highlights might be worth discussing.

Dr. Marshak:—Most patients with sprue will demonstrate alterations in the configuration of the small bowel as described previously. In a few patients, the small intestinal examination will be normal. Roentgen studies were performed on 46 patients with clinically proven sprue. In six patients, a normal small intestinal pattern was found. The remaining 40 patients exhibited in varying degrees dilatation, segmentation, fragmentation, hypersecretion and scattering of the barium column.

The impression of improvement in the small intestinal pattern in patients treated for sprue must be evaluated with care because marked variations in the appearance of the small intestine in sprue from study to study or even during the course of a single examination may occur. In our studies there is a discrepancy between the degree of clinical improvement under therapy and the roentgen changes observed. In only a few instances did the sprue lessen in intensity or disappear.

In 4 of 17 patients maintained on liver therapy, B_{12} or folic acid, the small intestinal pattern was returned to normal. Of 22 patients with abnormal small bowel studies receiving steriod therapy, two showed considerable diminution in dilatation and segmentation. In two others, segmentation and hypersection were reduced, however, dilatation persisted. We have had no experience with the effect of a gluten-free diet on the roentgen appearance of the small intestine.

In contrast to the alterations and the appearance of the small bowel in primary and some cases of secondary sprue the roentgen findings in pancreatogenous steatorrhea are essentially normal. In pancreatic lesions there is an absence of pancreatic lipase and the lipid content of the stool is made up primarily of neutral fats. In sprue the stools contain a large amount of fatty acids. Fatty acids are irritating substances which may cause the small intestine to respond with an overproduction of mucus. It has been shown experimentally that segmentation of the barium colon can be produced in normal individuals

by the introduction of fatty acids and mucus into the intestinal tract. This then may be the major factor responsible for segmentation in sprue. It is of interest that in patients successfully treated for sprue, fatty acids in the stool may be returned to normal levels, however, segmentation still persists. Therefore, although the fatty acids and mucus may be one of the contributing factors, other mechanisms such as the autonomic nervous system, altered chemical balance, infection may also play a role in the production of segmentation.

Dr. Lepore:—I am sure that the discussion might be prolonged endlessly. It is a fascinating field, and it is obvious that many things have happened since the days of Evan Evans. I happen now to occupy his office. He came down the day I entered his office and looked around, and we chatted about medicine, and he had some sprightly comments to make, at the age of 83, and then he said that medicine had certainly become much more complicated since his day. (Laughter and applause)

THE ALLERGENICALLY DENATURED DIET IN THE TREATMENT AND PREVENTION OF FOOD ALLERGY*

BRET RATNER, M.D.

New York, N. Y.

Under ordinary circumstances ingested food proteins are broken down into their component amino acids before absorption into the circulation. There is evidence, however, that unsplit proteins may enter the blood stream directly from the gastrointestinal tract in both normal and allergic persons[1].

When unaltered antigen enters the blood stream allergic antibodies may be generated and become attached to tissue cells. Subsequent ingestion of the same food antigen may produce allergic manifestations. The clinical allergic picture which develops depends on the site at which the reaction between the fixed tissue antibodies and the ingested antigen takes place. Thus, the symptomatology may occur in the gastrointestinal tract, the skin, the respiratory tract or the nervous system.

Sensitization does not occur readily. It would appear that there are certain conditions necessary for its fulfillment: 1. the protein fractions must be in a native state, soluble, dialyzable and of low molecular weight; 2. the intestinal tract must be particularly permeable at the time the food is ingested; 3. in general the quantity ingested appears to play a role.

There are two lines of defense against the invasion of unaltered food proteins into the blood stream. Food proteins are hydrolyzed by enzymatic intestinal digestion. The intestinal wall is generally regarded as being impermeable to the passage of colloids. Nevertheless, unaltered food proteins may at times traverse the wall of the intestine. After entrance into the circulation such proteins may be broken down by proteolysis or excreted via the kidney. The efficiency of these defense mechanisms varies in different individuals and even in the same individual may function adequately at one time and not another.

Defenses may fail as a result of actual pathologic conditions of the intestinal tract or because of increased permeability of the gastrointestinal wall characteristic of the newborn period and early infancy, and following severe gastrointestinal disturbances, convalescence from diarrhea, or periods of great strain or malnutrition.

The fetus may be sensitized to food proteins which the pregnant woman consumes in excess as a result of "cravings" which often appear in the latter

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From the Departments of Pediatrics and Pediatric Allergy, New York Medical College, Flower and Fifth Avenue Hospitals, New York, N. Y.

months of pregnancy[2]. The undigested proteins pass from the maternal circulation into the fetal blood stream and may produce sensitization. The newborn may become sensitized through occasional feedings of raw milk or raw egg, for example. Sensitization in older children and adults may result from ingestion of raw foods, fad diets, indulgence in seasonal foods and from bizarre foods eaten in excess periodically.

Food sensitivity may persist for years or tolerance may supervene. If soluble antigens enter the circulation in small amounts and at frequent intervals, a tolerance may be established.

Bearing these basic considerations in mind, it would appear that in order to prevent the inception of allergy, particularly in periods which we have described as vulnerable, our efforts must be directed to minimize the passage of unaltered proteins through the intestinal wall. It should follow, therefore, that if the ingested foods are not highly diffusible and are taken in moderate amounts, we may deter the development of allergic sensitization. Toward this end we have advocated the use of heat denaturation in order to minimize or eliminate allergenicity of foods in the prevention and treatment of food allergy[3]. This we term allergenic denaturation.

Allergenic Denaturation

Denaturation is used to designate the change of protein from a soluble to an insoluble form brought about by a large variety of chemical and physical agents including acids, alkalis, alcohol, acetone, salts of heavy metals, alkaloidal reagents and dyes, light, pressure and heat.

In relation to heat, Chick and Martin[4] define denaturation as the reaction between protein and moist heat which results in coagulation. One of the significant changes which occurs in denaturation of native proteins is its loss or diminution of specific immunologic properties. In this paper we are concerned with these antigenic alterations in respect to allergy.

It is evident that coagulated proteins are delayed in their passage through the gastrointestinal tract. Such delay permits more complete breakdown of the proteins, thus rendering them less antigenic. Furthermore such coagulated proteins diminish the probability that native undigested fractions will pass through the intestinal wall and act as allergens.

We therefore use the term allergenic denaturation to designate the changes which occur with the heat labile fractions, reducing or nullifying their capacity to induce allergic reactivity.

Denaturation by Moist Heat

Proteins in a dry or nearly dry state can be heated to a high temperature without antigenic change. It was shown that crystalline egg albumin suffers no

change by heating to 120°C for several hours in a dry state. According to Chick and Martin the coagulation of protein is not solely the effect of temperature. Moisture in the form of water or steam must be present, in addition, to coagulate proteins.

In the manufacture of dried milk by the spray method, the evaporation of the water content is practically instantaneous. Further application of heat to the dry powdered product does not alter the antigenicity of the protein fractions.

Our experiments[5] which demonstrate the absence of any change in the antigenic properties of milk which has been spray-dried lend further support to the concept that coagulation by heat can take place only in the presence of moisture.

The proteins in milk consist largely of lactalbumin and lactoglobulin found in the whey fraction, and casein in the curd. Some early investigators indicated that there was no apparent change in the antigenic properties of milk after heating to 100°C. Wells[6], however, pointed out that a distinction must be made between the heat labile and heat stable protein fractions and he attributed the early findings to the presence of casein which is heat stable. Cutler[7] demonstrated a definite antigenic change in the whey proteins of heated (evaporated) milk. Lewis and Hayden[8] corroborated the decrease in antigenic properties of the whey proteins in heated milks and also noted that no changes occurred in the casein.

Ratner and Gruehl[5] tested the antigenicity of milks modified by various heat procedures. In a series of anaphylaxis experiments in guinea pigs, we found that there was a definite loss of shock producing properties of the whey fractions. The casein components were apparently unaffected by heat.

When guinea pigs were fed heated milk, i.e. evaporated or boiled milk, as compared to raw milk, a marked reduction in the sensitizing ability of the whey proteins and a moderate reduction of the casein fraction were noted.

Ratner, Crawford and Flynn[9] showed that the majority (75 per cent) of milk sensitive children react to the lactoglobulin and lactalbumin fractions. Only 25 per cent are sensitive to the casein fraction. Since casein is precipiated in the stomach by pepsin and hydrochloric acid before proceeding into the intestine, the soluble allergens passing the pylorus to any great extent are the albumin and globulin fractions contained in the whey. Hence, a possible explanation may be offered for the more frequent sensitivity to the whey proteins of raw milk.

By subjecting raw milk to heat, the whey proteins become coagulated. Therefore individuals with sensitivity to lactoglobulin and lactalbumin can tolerate denatured milks such as Similac or other evaporated cow's milks, or

raw goat's milk. Persons sensitive to casein, which is unaffected by heat, however, cannot even tolerate denatured cow's milk or goat's milk. In such cases, a milk substitute such as Mull-Soy or other soybean preparations is indicated. It is interesting to observe that the whey proteins in goat's milk and cow's milk differ immunologically from each other whereas the casein is species nonspecific.

An individual sensitive to egg white will have reactions to a soft boiled egg but may tolerate hard boiled egg. The degree of coagulation is of importance. Maximum denaturation requires 30 minutes of boiling. In egg white there is present a heat stable fraction, ovomucoid, and a heat labile fraction ovalbumin, comparable to heat stable casein and the heat labile whey proteins in milk. Individuals sensitive to the ovomucoid fraction cannot tolerate even hard boiled egg.

We have also subjected several forms of cereal products to varying degrees and types of heat[10]. In some instances cereal grains were heated under 10 pounds of steam pressure for 20 minutes; in other instances they were treated with 22 pounds of steam pressure for as long as an hour or more. Breads and crackers were baked by dry heat. We learned that products such as bread, toast, crackers, biscuits, pancakes, waffles, pastries, cakes, piecrust and the majority of corn products remain allergenic. On the other hand, certain commercially dried cereals, which are all previously boiled, and home cooked cereals, are reduced in their allergenicity and produce little or no reaction in sensitized animals.

In animal experiments we determined that soybean is an innately weak allergen[11]. We demonstrated in the human subject that the allergenicity was retained in certain of the moderately heated preparations whereas the specially heat treated Mull-Soy was found to be nonallergenic[12].

A point of further interest is the relation of heat to the digestibility of proteins. Mendel and Lewis[13] and Bateman[14] showed that raw egg white is digested to only a small extent, whereas cooked egg white has a higher coefficient of digestibility. Furthermore, it was demonstrated by Sennewald et al[15] that boiled or evaporated milks are more rapidly digested *in vitro* by pepsin and trypsin than raw milk, the changes being in direct proportion to the amount of heat applied and the length of time of heating.

From this it may be gathered that, in general, heat labile proteins may be more readily broken down into harmless split products by enzymatic digestion and thus tolerated by allergic subjects.

The homogenization of evaporated milks, which produces extremely fine soft curds, is another factor which aids in minimizing the passage of unaltered proteins through the intestinal wall.

Cook et al[16] have studied the effect of heat on the nutritive value of proteins. They claim, from studies on rat growth, that there is a moderate lowering

of the nutritive value of proteins after heating. Such effect, however, is not marked and is perhaps of little significance. Schroeder et al[17] demonstrated in dogs that heated proteins retain their nutritive value.

Denaturation by Elimination of Antigenic Elements

In this form of denaturation, the actual protein elements are eliminated from the particular food. An allergenic change in a food by the physical elimination of antigenic elements is not denaturation in the accepted sense. For our purposes, however, we should also like to designate such foods for practical purposes as being allergenically denatured.

Ratner and Gruehl[18] made a study of the anaphylactogenic properties of malted sugars and corn syrups. In the conversion of starches into sugars, the cereal grains were subjected to enzymatic action. We found that the intermediary products such as Brewer's malt and malt extracts retained the antigenicity of the original cereal grains. When, however, the procedure was carried out to the final stage, the dextrimaltoses were shown to be completely devoid of antigenicity. The proteins had been eliminated from the final product by a process of boiling and filtration.

In relation to corn syrup, which was also nonallergenic, the protein elements had been eliminated by heat, acidification and filtration.

Further examples of denaturation by elimination of the protein elements were studied by Ratner et al. We found that reactions to orange were largely due to contamination with the seed protein and orange peel oil[19]. The seed was responsible for the true allergenicity and the peel oil had a primary irritant effect due to its toxicity. A brand* of canned orange juice which was devoid of both peel oil and orange seed protein proved to be nonallergenic[20]. Oil extracted from highly allergenic peanuts was shown to be completely devoid of peanut antigen and demonstrated to be nonallergenic in both the guinea pig and human subject[21]. This was also true for cod liver oil that was free from cod fish protein[22], cottonseed oil from which the cottonseed protein was eliminated and soybean oil, free of soybean protein[12].

In a study of gelatin[23] we found that the purified form† was nonallergenic. Gelatin itself, which is an incomplete protein, was found to be entirely devoid of allergenicity. In the precursors of gelatin there was a bovine serum contaminant which was allergenic. This contaminant was eliminated by heat, acidification and filtration in the preparation of the purified product. The bovine serum

*Bib orange juice.

†Knox IV Gelatin.

contaminant was occasionally found in the food grade gelatin but not in the intravenous grade.

Allergenic and Nonallergenic Foods

Whether the results obtained in experimental animals can be applied to food hypersensitivity in human beings will depend on further clinical experience. Based upon the experimental findings presented and our own clinical experience, we have classified foods, as they are presented for consumption, into the following categories.

We must caution that exquisitely sensitive individuals may not be able to tolerate a particular food even though it has been found experimentally to be allergenically denatured.

This classification has formed the basis of our management of patients who are specifically sensitive to one or another food. An individual sensitive to a particular food either eliminates that food from his diet or substitutes it with the nonallergenic form.

Allergenically Denatured Foods	*Allergenic Foods*
Similac and other evaporated milks.	Raw, pasteurized, spray-dried milk, buttermilk, yogurt, other acidified milks and milk-containing foods.
Hard boiled eggs (30 minutes).	Raw, soft-boiled, scrambled, fried eggs, egg-containing foods and drinks.
Commercially precooked and home-boiled cereals.	
Melba toast, Rye Krisp, Triscuits, Zwieback.	Breads, crackers, biscuits, waffles, pancakes, pastries, etc.
Boiled spaghetti and noodles.	
Boiled meats and poultry.	Rare roasted meats and poultry.
Boiled vegetables and juices.	Raw vegetables and juices.
Boiled fruits and juices, Bib orange juice.	Raw fruits and juices.
Soups	Fish
Mull-Soy	Nuts
Knox gelatin	Chocolate
Edible oils	Condiments

Although no experimental work has appeared in reference to meats, fruits, vegetables from this aspect, on the basis of our clinical experience we feel that cooking as indicated in the table probably results in heat denaturation. On the other hand, fish, which is a frequent offender, does not appear to be antigenically altered by the application of moist heat. This was demonstrated by

Prausnitz and Küstner[24] in their original paper in which they described the presence of circulating antibodies by a method now known as the Prausnitz-Küstner Reaction.

Uses of the Allergenically Denatured Diet

This diet may be used in 1. the course of study of a patient whose specific food sensitivities are not known and 2. in the treatment of a patient whose specific food sensitivities are known.

1. The procedure we follow is to put a patient on a completely allergenically denatured diet when our studies are initiated. As an adjunct to the usual skin testing, the allergenically denatured diet serves a useful purpose for several reasons. If the allergic condition clears it is evident that such a patient is sensitive to one or more of the heat labile food proteins or fractions. If the condition does not clear it must be assumed a) that the patient is sensitive either to heat stable fractions of the food, or b) is sensitive to a food plus other factors such as pollens, inhalants, contactants, molds or bacteria, or c) is sensitive to these latter allergens alone and not to a food.

2. After the diagnostic procedures are completed and the specific food sensitivities are determined, only those foods to which the patient has been found sensitive should be eliminated, or given in allergenically denatured form providing the patient is sensitive to the heat labile fractions. The elimination of a particular food or giving it in a denatured form should be continued for at least a year. The food should then be introduced in undenatured form in small amounts. Elimination of a food is often followed by a loss of sensitivity and the reintroduction in small amounts after a year's abstinence may result in the establishment of tolerance. Certain cases, however, may require a longer period, or others remain fixed.

Foods in denatured form serve also in the prevention of food allergy.

During pregnancy, for example, the pregnant woman whose appetite often becomes inordinate can take part of her food in denatured form and thus minimize the possibility of the passage of unaltered protein into her blood stream.

The prevention of food allergy in early infancy rests largely on the use of denatured foods. This is common practice amongst pediatricians for about 85 per cent of infants today are fed Similac or other forms of evaporated milk, are given hard boiled eggs, cooked cereals, boiled meats and vegetables, etc. In my estimation, this practice has brought about a marked reduction in allergy to milk, egg and cereals.

The prophylaxis of food allergy arising in other vulnerable situations, e.g. convalescence from intestinal disturbances and debility, is aided as well by the use of allergenically denatured foods.

Allergenically Denatured Diet

Foods Allowed	*Foods Not Allowed*
1. *Milk and Beverages*: Similac or evaporated milk; milk substitutes such as Mull-Soy; additions to milk such as dextri-maltose, corn syrup and cane sugar. All bottled soft drinks, coffee, tea.	1. *Milk*: Raw, pasteurized, spray-dried buttermilk, yogurt and other acidified milks, butter, cream, cheese, ice cream, white bread containing milk, puddings containing milk, waffles, pancakes, milk shakes, chocolate milk, milk sodas.
2. *Eggs*: Only 30 minute hard boiled.	2. *Eggs*: Raw, soft boiled, scrambled, fried, poached, coddled; all foods prepared with egg as ice cream, cake, sherbets, pastries, glazed breadstuffs, puddings, egg drop, mayonnaise, bonbons, egg-containing confections, waffles, pancakes, meringues, egg nog, egg drinks.
3. *Cereals*: All home cooked and commercially precooked cereals; cereal foods such as spaghetti, macaroni, noodles.	3. *Cereals*: None
4. *Breadstuffs*: Only Melba toast, Triscuits, Rye Krisp, Zwieback.	4. *Breadstuffs*: Bread, crackers, cake, biscuits, toast, pretzels, pastries, waffles, pancakes.
5. *Meat and Poultry*: Boiled or stewed only (beef, lamb, veal, pork, chicken, turkey).	5. *Meat and Poultry*: Rare meats and poultry, glandular meats, smoked or salted meats, roasted, pan fried, broiled, baked.
6. *Fish*: None	6. *Fish*: All fish.
7. *Vegetables*: All boiled vegetables and juices.	7. *Vegetables*: All raw vegetables and juices.
8. *Fruits*: All cooked or stewed fruits, grape juice, cranberry juice, Bib orange juice, boiled fruit sauces.	8. *Fruits*: All raw fruits and juices except Bib orange juice.
9. *Soups*: All clear soups and all other soups whose ingredients are thoroughly cooked. Do not add seasoning, bread, parsley, crackers, cheese, egg drop after the soup has been cooked.	9. *Soups*: Cream soups.
10. *Desserts*: Knox gelatin, stewed fruits, puddings without egg and made with Similac or evaporated milk, ice cream made with evaporated milk.	10. *Desserts*: Cake, pie, pastries, ice cream, cookies, sherbets, puddings, (except those made with evaporated milk and devoid of egg).
11. *Edible Oils*: Peanut, cottonseed, and corn oils, vegetable shortening, lard, olive oil, oleomargarine.	11. *Edible Oils*: None
12. *Nuts*: None	12. *Nuts*: All nuts.
13. *Chocolate*: None	13. *Chocolate*: All chocolate and chocolate-containing foods, cocoa.
14. *Miscellaneous*: Hard candies, jellies, marmalade, syrups.	14. *Miscellaneous*: Candies (except hard), flour-thickened gravies, poultry stuffing, condiments except salt.

Ascorbic acid in adequate dosage should be given if a completely denatured diet is used.

Whatever its shortcomings, we believe that this diet is more advisable than elimination diets[25]. It does not deprive a patient of essential food elements, with the exception of Vitamin C which must be added.

Summary

Foods may be allergenically denatured primarily through the use of adequate heat in the presence of moisture or by physical elimination of antigenic elements.

Allergenic heat denaturation is largely a process of the coagulation of the heat labile fractions of the protein elements. Coagulation delays the passage of proteins through the gastrointestinal tract, encouraging enzymatic digestion. Thus heat denaturation minimizes the passage of unaltered proteins through the gastrointestinal wall into the circulation, on the one hand deterring the development of allergic antibodies and the establishment of hypersensitization, and on the other, reducing the incidence of hypersensitive reactions to foods to which the patient has already been sensitized.

The allergenically denatured diet is of value in the prevention of the inception of food allergy of the infant during pregnancy, during the newborn period and infancy, and during convalescence from gastrointestinal disturbances, debility and periods of excessive food intake.

A knowledge of the principles underlying an allergenically denatured food is invaluable in the management of patients suffering from food allergy.

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Discussion

Dr. I. Snapper:—Dr. Ratner has brought up the all important point that the allergenic factors of many foods can be considerably diminished by cooking. We have to remember that nowadays nearly all our food is denatured, not only by boiling, but also by the addition of different substances. This holds true even for the "reinforcing" of our vitamins. Nearly all our vitamin mixtures contain Vitamin B_{12}. It is considered probable that Vitamin B_{12} stimulates the growth of malignant tumors, but nevertheless large doses of vitamin mixtures are given to patients with a neoplastic disease. One cannot eat chicken anymore if one is allergic to aureomycin because this antibiotic is fed to chickens to make them get big and fat in a short time. Unexplained changes of the mucous membrane of the mouth have cleared up after the meat of aureomycin-fed chickens has been eliminated from the diet.

Even the evaporated milk which Dr. Bratner discussed may be denatured as is evidenced by the following experience.

Since the dangers of the administration of excessive doses of Vitamin D are common knowledge, hypervitaminosis D in adults has become a rarity. In infants, however, at least in the United Kingdom, a new syndrome "idiopathic hypercalcemia" which may well be due to hypervitaminosis D, has now been recognized. A recent report mentions that between 1953 and 1955, 204 such patients have been observed, mainly infants between four and eight months of age.

In the malignant form of this disease dwarfism, mental retardation, microcephaly and cerebral signs are present. The benign form of the disease is reversible and is of considerable clinical importance. The children with benign idiopathic hypercalcemia usually suffer from loss of appetite, tenacious vomiting and constipation. Often a systolic murmur can be heard either at the point of maximal impulse or all over the precordium. Hypercalcemia and hypercalciuria are constant findings, the serum phosphorus and alkaline phosphatase remain usually normal, blood urea nitrogen and cholesterol are increased. Under adequate treatment these abnormal values rapidly return to normal and the systolic murmur disappears.

Nephrocalcinosis has been frequently observed. Linear deposition of abnormally dense bone near the epiphysis of the long bone and osteosclerosis of skull base and vertebral bodies may be present.

There is strong evidence that hypervitaminosis D may play an important role in the etiology of this syndrome. "National Dried Milk", a popular food for infants in the United Kingdom, contains "not less than" 1,200 I.U. of Vitamin D per reconstituted liter, probably more. The Vitamin D content of several other milk preparations, used for infant feeding in England, is even higher. The "British National Cod Liver Oil Compound" contains not less than 700 to 800 I.U. Vitamin D per teaspoonful, probably more. Cereals are also fortified and some brands contain 1,500 I.U. per ounce. Infants who receive 1.5 pints of reconstituted dried milk, 1 ounce of fortified cereal and one teaspoon of fortified cod liver oil may easily ingest about 4,000 I.U. of Vitamin D per day. This intake is far in excess of the 400 to 700 I.U. which around 1940 was recommended as the daily intake for infants. The daily maximal intake of Vitamin D for infants was usually considered to vary around 1,500 I.U.

In this connection it is of interest that in the United States no case of idiopathic hypercalcemia has been reported yet. In our country the most popular brand of evaporated milk contains only 420 I.U. Vitamin D per reconstituted liter. The possibility, however, that cases of hypervitaminosis D in infants and children may also develop in the United States exists, since certain halibut liver preparations used in this country, contain 6,000 I.U. Vitamin D per teaspoonful.

Breastfeeding has not yet become obsolete in England and it is interesting that until now no case of idiopathic hypercalcemia in breastfed infants has been

reported. The vitamin content of human milk varies between 50 and 100 I.U. Vitamin D per liter, that is only 25 per cent of the Vitamin D content of cow's milk.

In most cases of idiopathic hypercalcemia feeding with low calcium milk powder (Locasol) and low calcium cereal (Glaxco) boiled in distilled water, brought rapid recovery. In other cases cortisone, mainly by inhibiting calcium and phosphorus absorption from the intestine, has been very helpful.

The British Pediatric Society has now decided to recommend that no foods fortified with Vitamin D should be given to infants at all. Every infant, however, should receive cod liver oil of known potency. This of course is exactly the same nutritional formula which was customary half a century ago.

Therefore it is well to remember that we have no normal, natural food anymore because many of our nutrients have been "improved".

Now, the fundamental difference between food allergens and inhalation allergens is well demonstrated by the experience that food allergy cannot be detected by skin testing, in contrast to inhalation allergy which is often revealed by skin testing.

Food, by necessity, after absorption in the intestine, passes through the liver. During the passage through the intestine and the liver the chemical constitution and even the antigenicity of the nutrients is completely changed. In case a food allergy develops, the hypersensitivity is directed against a degradation product of the nutrient,—not against the original nutrient which is used for skin testing. Inhalation allergens go through the trachea and are rapidly absorbed in unchanged condition. There is no surface in the body which absorbs more readily than the tracheal mucous membrane. The latter absorbs even much more quickly than the intestine.

After the first World War when the French had very little strychnine left, at one of the veterinary schools a horse had to be killed. Since no strychnine was available it was decided to run water into the tracheal tube which the horse was carrying in order to drown the horse. To everybody's surprise, the trachea absorbed the water so quickly that the horse survived.

That shows how rapidly the trachea absorbs. Inhalation allergens are not changed before they are absorbed in the blood through the airways, food allergens are catabolized by the liver. Inhalation allergens can therefore be used for skin testing, unchanged nutrients cannot.

We have to thank Dr. Ratner for bringing this important subject before us. He is certainly right in his conclusion that patients who are allergic to certain foods may be able to take the foods after they have been changed by boiling or cooking.

Dr. Ratner:—Heat denaturation is part of our modern development of eating habits. Today the child is started with early solid foods. This could be done only in this era, because most of our foods today are heat-denatured. The same child 20 or 30 years ago, given an excessive amount of raw milk, raw egg, often developed allergy. Today most infants are fed evaporated milk or Similac, and hard boiled eggs with consequent reduction in allergy to these foods.

We sometimes get a celiac disease patient and put him on a denatured diet. At times one is surprised to discover that he does not have celiac disease but has a food allergy.

All hospitalized patients should be given denatured diets. Every doctor should know that a French fried potato is more digestible than a boiled potato, a hard boiled egg is more digestible than an eggnog, soup is more digestible than raw juices, etc.

As to the question of skin testing, to which Dr. Snapper referred, one does not usually get positive skin reactions with true food allergy relegated to the gastrointestinal tract.

The use of a denatured diet provides a balanced diet and one which is highly nutritious. If a doctor had a case of eczema and would cut out milk, egg, wheat and other essential foods, that child very often developed malnutrition and nutritional edema. With the use of the heat denatured diet, you can really have a very sanguine time about the management of many unknown conditions in the gastrointestinal tract. Its use will help tremendously in the prevention and treatment of food allergy.

PERSONALITY AS A FACTOR IN THE STUDY OF AUTONOMIC FUNCTIONS*

RALPH EICHHORN, M.D., F.A.C.G.

and

JACK TRACKTIR, Ph.D.

Houston, Texas

Numerous investigators have studied the effect of emotion upon the autonomic nervous system. Nowhere has this relationship been more intensely investigated than in the gastrointestinal system. The results collected painstakingly by smoked drum, balloon, tambour, strain gauge and manometer, etc., have led to a bewildering confusion of conflicting data, conclusions, results and assumptions.

Cannon's emergency hypothesis states that the emotions of anger and fear are essentially undifferentiated physiological states and as applied to gastric function are inhibitory in effect[1]. Alvarez states flatly that gastric secretion is decreased or stopped entirely by unpleasant or painful emotions[2]. Conversely, experimental findings by Mittelman and Wolf[3] imply that unpleasant emotions seem to augment rather than inhibit secretion in certain cases. Wolf and Wolff in their extensive study of their subject "Tom" report acceleration in gastric function associated with a reaction of internal conflict "with an unfulfilled desire for aggression and fighting back"[4]. Another investigator, Witkower, reported that hypnotically induced fear states brought about increased acid secretion in some subjects and decreased secretion in other subjects[5]. Whichever change occurred was consistent for each subject. This latter conclusion agrees more closely with our results.

There are three basic difficulties inherent in these studies. First there is an inability to define the emotions involved. Secondly there is failure to assess the personality dimensions of the subject. Finally there is the difficulty of translating life situations to laboratory conditions.

It is obvious, as Ivy points out, that in animal experimentation it is impossible to state with any degree of certainty the emotion experienced by the animal subject[6]. One animal subjected to repeated electric shock, or other similar stimuli, may become enraged, a second fearful, a third may exhibit a combination of emotions. This same criticism may be levelled at stimuli attempting to elicit specific reactions in humans. Whereas the subject may be enraged

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From the Department of Physiology, Baylor University College of Medicine, Houston, Texas.

at a particular situation presented such as "Tom" in Wolf and Wolff's study, this reaction may well be tempered by fear, by embarrassment at revealing intimacies of his situation or by the numerous other emotions that affect our responses. True, rage may well be a dominant emotion but can we be even fairly certain of this? This deficiency has been well recognized by most investigators and they speak ordinarily of "dominant" emotions. This must, by definition, represent a mixed emotion and be relatively unsatisfactory for experimental purposes.

Secondly, although one patient may react to a specific emotion with a specific response, will all persons react to this emotion with this same specific response? The answer is obviously, no. Physiologists have proceeded along the simple lines of stimulus and response fundamentally unsuited to study of the more complex problems involved in human emotion and behavior. A muscle is subjected to a stimulus and a simple twitch results. This is predictable and reproducible. We have come to expect the invariable result. One need only apply a specific stimulus and measure or titrate the result. This works with the central nervous system and where simple reflex arcs are involved. When one deals with the autonomic nervous system, however, a more complex chain of afferent reactions involved; one which is dominated by the reaction pattern of the individual. Witkower recognized this when he investigated the effect of emotion upon numerous autonomic functions and divided his subjects into various reaction pattern groups. He states "the manner of reaction is personally and typically determined"[5], and he classifies his subjects into plus and minus types differentiated by means of the secretory behavior of the salivary and gastric glands under the influence of emotion. He did not, however, correlate these plus or minus types with known reaction types. This division therefore was in terms of the individual's response pattern rather than upon the individual's personality projection.

The difficulty of translating a life situation to laboratory conditions was realized many years ago by Heyer[7]. He noted that the unpleasantness of the experimental method using a stomach tube led to unpredictable results. The subject, seated seminude and hungry in a strange laboratory filled with unusual instruments and dripping recording devices from every orifice, is given a carefully prepared interview. The recording device is set in motion and the individual supposedly registers a response to hate, fear or love. To avoid such absurdities Heyer used hypnosis so that the patient was unaware of passage of the tube or its presence during the experimental recording. He did not standardize his experiments, however, and did not study the effect of hypnosis alone.

These experiments were intended as a pilot device to seek a method whereby the difficulties inherent in the above resume might be minimized and also to introduce personality as a dimension to be measured in analyzing data.

Method

A group of 24 male subjects were subdivided into three anxiety groups, high, middle and low on the basis of Taylor's Manifest Anxiety Scale[8]. The total group was subjected to six experimental conditions: prehypnotic, hypnotic, post-hypnotic and hypnotically induced states of fear, anger and contentment.

By gastric intubation specimens of fasting gastric secretion were obtained from the subjects at 15 minute intervals during a 90-minute period for each

TABLE I

Medians for the Three Anxiety Groups (N=8) Under the Experimental Conditions for Each Measurement

	Hypnotic	Anger	Fear	Contentment
		Free Acid		
High Anxiety	24.3	16.7	54.2	45.8
Middle Anxiety	22.1	13.5	8.6	47.1
Low Anxiety	20.1	28.2	11.4	54.9
		Total Acid		
High Anxiety	37.8	27.5	64.5	59.3
Middle Anxiety	32.3	27.5	18.6	70.9
Low Anxiety	40.1	41.3	22.8	74.2
		Volume		
High Anxiety	13.4	5.5	8.6	9.5
Middle Anxiety	8.9	7.2	10.3	7.5
Low Anxiety	9.4	11.5	7.7	11.1
		Pepsin		
High Anxiety	2.4	3.5	3.3	2.4
Middle Anxiety	2.3	3.8	4.2	2.4
Low Anxiety	2.2	3.1	3.6	2.5

experimental condition. Measures of gastric secretion included free acid, total acid, volume, pepsin, bile and consistency.

A card-sorting task was used as an independent criterion of the hypnotically induced emotional conditions. An analysis of variance design with ranked data was used to test the reliability of differences between card-sorting scores, differences between the six experimental conditions on the measures of gastric secretion, the differences between the three nonemotional conditions on the measures of gastric secretion, and the reliability of the interactions between anxiety

groups and the four hypnotic conditions. The "T" test was used to find the reliability of differences between the prehypnotic and posthypnotic conditions on the gastric secretion measurements and the differences between hypnotic conditions on volume and pepsin measurement.

Results

The data for the three anxiety groups on four measures of gastric secretion are summarized in Table I.

The medians for the free acid secreted by the high and low anxiety groups under fear, anger and contenment conditions for a 90-minute period is shown in Figure 1.

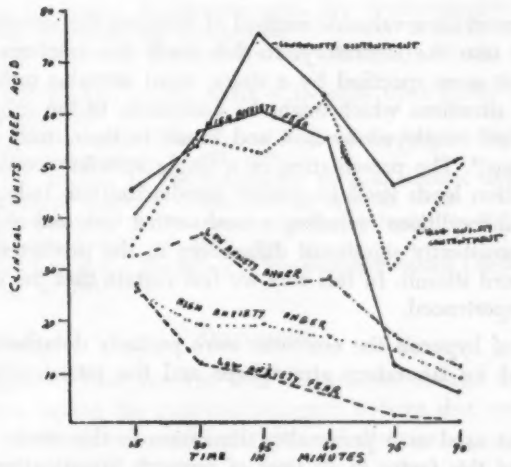

Fig. 1—Free acid secreted by the high and low anxiety groups under fear, contentment and anger conditions for the total experimental period.

The figures for total acid follow the pattern for free acid. The figures for volume secretion show no statistically significant interaction for the anxiety groups under these conditions.

The high anxiety groups showed a marked rise in acid secretion under conditions of fear. The low anxiety group showed a drop in acid secretion under the same condition.

The high anxiety group showed a fall in acid secretion under conditions of anger whereas the low anxiety group showed a rise in acid secretion under the same condition. This rise does not approach the high level reached by the high anxiety group under fear however.

Under conditions of contentment both groups show a rise in acid secretion and also in peptic activity.

There was a tendency for all of the curves to show a downward slope during the experimental period which may represent the subjects' inability to maintain the suggested emotion over such an extended period.

A more detailed and comprehensive description and analysis of our methodology and results is available in our original publications[9,10,11]. This paper is intended, however, primarily to stress the importance of considering personality dimension, in this case anxiety, as a factor in the study of autonomic function and to present a method whereby the difficulties inherent in such study may be minimized.

Comment

Hypnosis provides a valuable method of bringing the investigation of emotional behavior into the laboratory. In this study the emotions of fear, anger and contentment were specified by a single word stimulus rather than by the presentation of situations which might be anomalous to the subject. In essence this is the method employed by Bull and Frank in their study of hypnotically induced emotions[12]. The presentation of a single stimulus word to indicate an emotional situation lends itself to greater standardization. Independent criteria of the emotional conditions including a card-sorting task and objective observation showed consistently significant differences in the predicted directions between single word stimuli. In this way we feel certain that the desired emotion was actually experienced.

By means of hypnosis the emotions were partially detached from the conflict engendered by laboratory atmosphere and the introduction of a gastric tube.

Anxiety was used as a personality dimension in this study because of the predominance of this factor in all lines of research investigating the psychosomatic aspect of gastrointestinal disease. There is evidence for example from the studies of the personalities of ulcer patients that chronic anxiety plays an important role in the etiology of peptic ulcer. Physiologists in general have been impressed with the state of anxiety found in peptic ulcer patients who hypersecrete gastric juice[13]. Anxiety has also been implicated in the pathogenesis of regional ileitis, ulcerative colitis and other colonic dysfunction. When the results found in this study were broken down into the three anxiety groups certain differences became evident in gastric secretory responses to fear, anger and contentment and there is a clear differentiation between the effects of these emotions among these groups.

Conclusion

These results strongly suggest that future investigations of emotions as affecting autonomic functions should take into consideration various personality

predispositions of the subject. One that has been demonstrated by the present study is anxiety.

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Discussion

Dr. I. Snapper:—I have listened with the greatest interest to Dr. Eichhorn. Even the skeptics among the gastroenterologists believe that emotions have an influence upon gastroenterological functions and diseases.

This morning Dr. Hinton reminded us of Dr. Cushing's experiments which explain ulcer formation developing after a brain operation. We are acquainted with the gastrointestinal hemorrhages after laparotomies during which the intestinal tract was not touched. We are aware of ulcerative colitis, which sometimes occurs after operations which have nothing to do with the intestinal tract, for instance, after gallbladder operations. We are convinced that stress may cause organic lesions via the autonomic reactions of the gastrointestinal tract or at least that lesions can be so much aggravated that ultimately clinical symptoms and signs occur.

Thus, we are thankful for the experiments of the psychiatrists who prove how correct Goethe was when he defined science as "the artistic exhibition of facts".

GASTRIC POLYPS AND THEIR RELATIONSHIP TO CARCINOMA OF THE STOMACH

Review of Literature and Report of 65 Cases

AARON PLACHTA, M.D.

and

FRANCIS D. SPEER, M.D.

New York, N. Y.

It is the purpose of this paper to describe the pathology of 65 cases of gastric polyps from both autopsied and gastrectomized patients. On the basis of this study we intend to show that malignant transformation of a benign polyp is very rare, if in fact it ever occurs.

Some students of intragastric tumors stress the precancerous character of adenomatous polyps, pointing to the high incidence of gastric polyps associated with gastric malignancy in support of their contention. A review of the literature makes it apparent that the incidence of polyps of the stomach, whether benign or malignant, is difficult to determine and that benign intragastric pedunculated polyps are rare. To illustrate this rarity Borrmann[2] reported one case in 11,475 consecutive autopsies.

Stout[40] voiced his observation as to the common occurrence of adenomatous polyps in the large bowel as compared to the rarity of such lesions in the stomach. He felt that adenomatous polyps may become malignant but their rarity accounts for extremely few carcinomas arising in a benign gastric polyp of the stomach.

Pearl and Brunn[32] reported an incidence of 51 per cent malignant gastric ulcers in 41 cases of gastric polyps, yet failed to demonstrate in a single example transitional changes in the polyps. Spriggs'[37] cases were followed for 12 years without any apparent transformation. Over a period of years Rigler and Ericksen[34] observed a number of patients in whom no evidence of malignancy developed.

Carey and Hay[4,5], reporting a large series of gastrointestinal tumors, referred to the malignant transition of a benign gastric polyp. The patient was a 75-year old woman. The transition was interpreted clinically on the basis of increased size, burning sensation of many years' standing. The lesion was resected and found microscopically to be a benign adenomatous polyp of the stomach.

From the Department of Pathology and Clinical Pathology, New York Medical College, Flower and Fifth Avenue and Metropolitan Hospitals, New York, N. Y.

Wechselman[43] and Doering[9] supported Meulengracht's[28] contention that one-half or more of intestinal polyps undergo malignant degeneration, but insisted that such change in the lesions located in the stomach is exceedingly rare, if it ever occurs. Balfour and Henderson[1] found such degenerative changes in only 3.5 per cent. Stewart[38], in 11,000 necropsies, disclosed associated carcinoma in only three instances, and in these it was uncertain that the malignant process had originated in a polyp. Carman[6] detected two cases in 50,000 x-ray examinations of which one was that reported by Balfour[1].

Miller and associates[23] collected 24 carcinomatous gastric polyps from the literature, adding eight cases of their own. In no instance of the eight cases regarded as carcinomatous polyps was there evidence that the lesion began as

TABLE I

COLLECTED AND PERSONAL INCIDENCE OF ADENOMATOUS GASTRIC POLYPS IN CONSECUTIVE AUTOPSIED PATIENTS

Date	Authors	No. of Autopsies	Adenomas	Incidence
1931	Stewart[38]	12,800	56	0.4
1935	Lawrence[18]	7,000	50	0.7
1936	Rigler and Ericksen[34]	6,242	49	0.8
1940	Buckstein[3]	21,026	76	0.4
1941	Spriggs and Marxer[37]	4,400	11	0.25
1951	Yarnis, Marshak and Friedman[44]	8,735	30	0.29
1956	Plachta and Speer	14,620	52	0.36
	Total	74,823	324	Mean 0.43

The over all adenomatous gastric polyp incidence in both collected and personal cases in consecutive autopsied patients indicates the mean incidence of benign gastric adenomas to be 0.43 per cent of a combined total of 74,823 autopsies.

a benign polyp. There was no evidence, gross or microscopic, to substantiate the authors' claim of carcinoma arising in a benign gastric polyp.

Niemetz and Wharton[30] collected 32 cases from their files. Eight of their patients were subjected to gastrectomy, and lesions studied microscopically proved to be benign adenomatous polyps. Disclosure of benign gastric polyps was also noted by them in nine autopsied patients. In none of the lesions in their series did they encounter malignant degeneration of a benign gastric polyp.

Paul and Logan[31] felt that the transition from benign polyp to carcinoma was yet to be observed. Single polyps have yet to show distinct transition

whereas the reports to date of transition to carcinoma in adenomatous single or multiple polypoid lesions have indicated their primary initial malignancy.

Material

The study which forms the basis for this report consists of 635 gastric neoplasms collected from the Flower and Fifth Avenue and Metropolitan Hospital files of 14,620 consecutive autopsies. Of the 635 gastric neoplasms, 493 were malignant and 142 were benign gastric tumors.

Of these benign tumors 52 were adenomatous polyps, 3 carcinoids, 55 leiomyoma, 6 lipoma, 5 fibroma, 7 inflammatory polyps, 2 hemangioma, 3 eosinophilic granuloma, 3 dermoids, 4 neuroma and 2 were neurofibroma.

The surgical files contributed 33 surgically explored patients with gastrectomy and removal of the benign gastric tumors. Of these tumors 13 were adenomatous polyps, 1 carcinoid, 14 leiomyoma, 2 fibroma, 2 inflammatory polyps and 1 eosinophilic granuloma.

It is the group of 65 patients, both autopsied and operated upon, in whom benign lesions classified as primary adenomatous gastric polyps both sessile and pedunculated, single or multiple, were found that we are concerned with in this paper (Tables I, II and III).

The combined group of 65 patients, both men and women, ranged from 19 to 88 years of age. Fifty-two of the patients were medically observed. There were three of these patients in whom the cause of death was directly attributed to the complications of the large adenomatous polyps terminating in obstruction, hemorrhage or gangrene of both polyp and duodenum. Two patients were followed for periods of 18 and 23 years, respectively, in whom the terminal clinical pictures were regarded as typically malignant. In the other 47 patients the gastric polyps were accidental autopsy findings.

Three autopsied postgastrectomized patients survived 8, 10 and 12 years. The causes of death, respectively, were: arteriosclerotic heart disease; myocardial infarction, acute; arteriolar nephrosclerosis terminating in uremia. Of the remaining 10 gastrectomized patients, 6 patients are alive and well, 4 patients survived 2, 13, 15 and 18 years following surgery. No autopsy was obtained in any of the 4 cases, but their death was attributed, respectively, to: hypertensive heart disease; pyelonephritis with sepsis; bilateral pneumonitis, diffuse; arteriosclerosis, generalized, with myocardial infarction. This combined group, therefore, consists of 55 autopsied patients, 4 gastrectomized patients who are dead and 6 gastrectomized patients who are alive and well and under observation at this time.

Clinical Features

Follow-up observations consisted of semi-annual or yearly examination of periods from 19 months to 23 years. Patients with benign gastric polyps did

not have the diagnosis changed regardless of the number of subsequent examinations.

Achlorhydria was present in 95 per cent of the 13 gastrectomized patients. In 7 of the cases, hematemesis occasioned the patient to seek hospitalization. In each instance there was associated melena and hypochromic anemia. In 5 of the cases there was epigastric pain, nausea, vomiting, anorexia and weight loss. Of the autopsied patients the disease remained symptomless for years or a lifetime in 80.7 per cent of the cases. In 2 of the patients there was recent

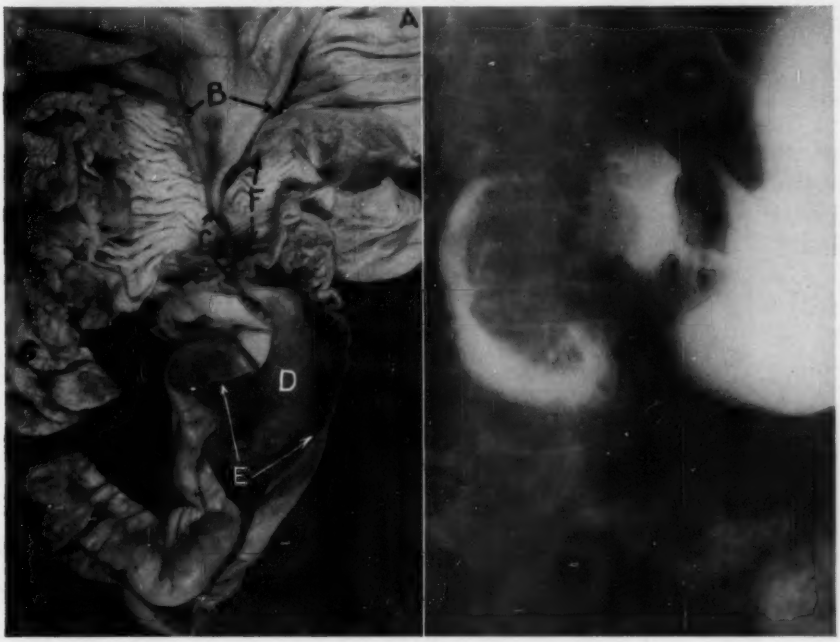

Fig. 1a Fig. 1b

Fig. 1a–Type of tumor producing the "ball-valve-syndrome". A. Stomach, antral and pre-pyloric regions. B. Triangular drawn-out pedicle overlapping the pyloric ring. C. Contiguous elongated pedicle extending into the lower portions of the duodenum. D. Telescoped infarcted polyp. E. Infarcted small bowel. F. Accordion-type constriction of the 1st and 2nd portions of the duodenum. G. Pancreas.

Fig. 1b–Telescoped polyp into duodenum producing deformity of pylorus and accordion constriction of duodenum.

nausea, moderate discomfort over the midepigastrium behind the sternum, flatulence and some giddiness. Achlorhydria was present in the 3 cases tested.

In 3 of the patients the "ball-valve-syndrome" typical of pedunculated intragastric tumors of the stomach situated near the pylorus was illustrated.

These patients had repeated, paroxysmal, spasmodic attacks of gastric pain accompanied by temporary prostration, anorexia, anemia, hematemesis or melena, and rapid loss of weight. This was due to temporary enveloping of the tumor and its pedicle by the pylorus. When freed, the patients' symptoms subsided, they rapidly improved and continued in good health until another attack occurred, caused by the ball-valve action of the pedunculated tumor closing the pylorus. During the last admissions, relaxation did not take place, obstruction and infarction of both tumor and duodenum occurred resulting in

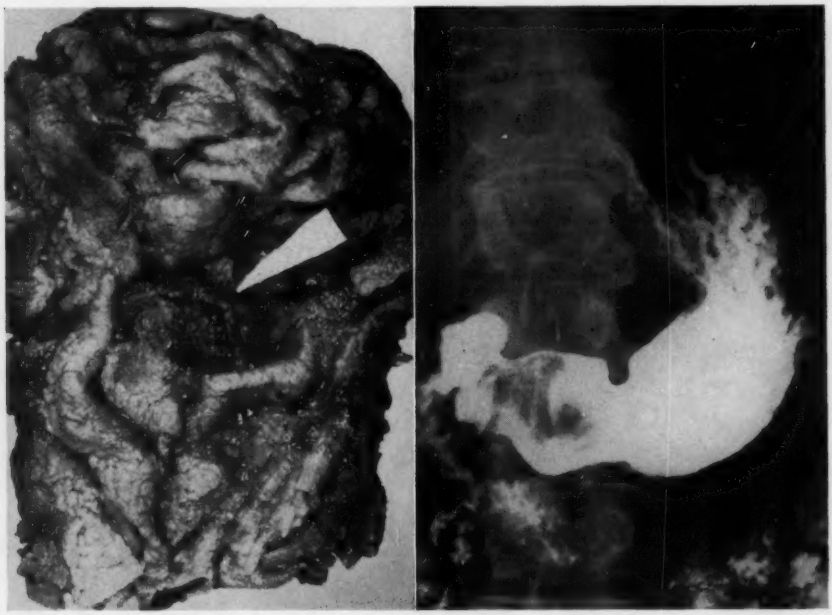

Fig. 2a Fig. 2b

Fig. 2a—Pedunculated adenomatous polyp with irregular roughened periphery, surrounded by severe hypertrophied gastric mucosa.

Fig. 2b—Conspicuous filling-defect with central cyst-like deformity.

hemorrhage and gangrene of both adenomatous polyp and bowel (Figs. 1a, 1b, 3a and 3b).

X-ray Features

The roentgenographic findings in one patient showed obstruction of the cardia with diffuse dilatation of the esophagus. Nine patients showed filling defects in the pyloric end of the stomach, creating an unusual conspicuous appearance interpreted as cancer (Fig. 2b), or central cyst-like deformity suggestive of an ulcer. Three patients showed defects on the anterior and

posterior wall of the stomach, either circumscribed or punched-out in appearance, or filling defects leaving the curvature regular and pliant. Two patients with small gastric tumors situated near the pylorus prolapsing into the duodenum produced a deformity of the cap which resembled that caused by a duodenal ulcer. In three patients the prolapsed, telescoped large polyp produced an accordion constriction of the first portion of the duodenum and jejunal junction producing a deformity and filling-defect (Fig. 1b). There were

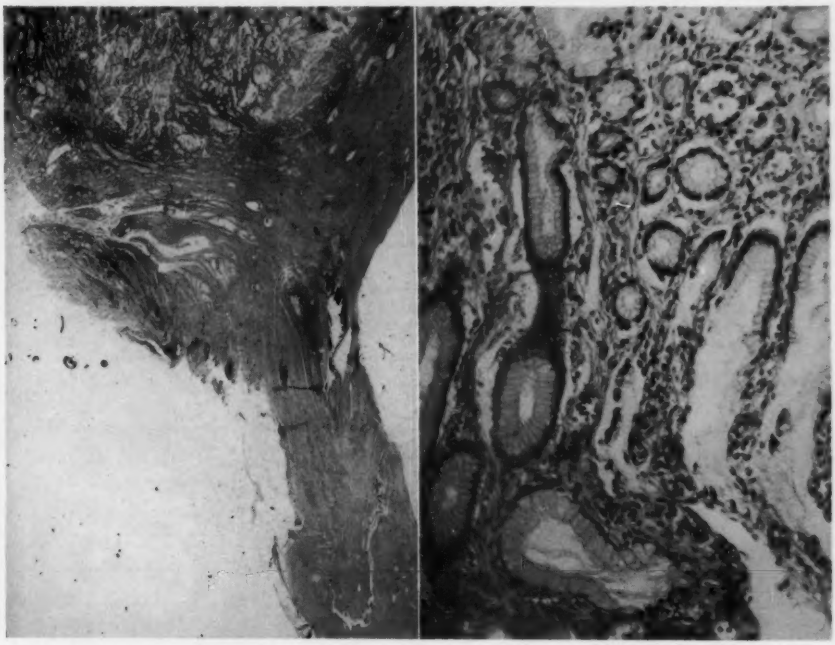

Fig. 3a Fig. 3b

Fig. 3a–Low power view of large pedunculated adenomatous polyp showing a conspicuous pattern of mucus secreting glands, advanced microcystic transformation associated with cellular hyperchromatism without alteration of the glandular pattern and severe intestinal metaplasia.

Fig. 3b–Higher magnification showing disappearance of gastric glands, intestinal metaplasia and chronic inflammatory activity.

no roentgenographic signs pathognomonic of benign gastric tumors, although certain findings were strongly suggestive of their presence.

Gastroscopic Features

The gastroscopic features in patients with benign adenomatous polyps were those of a flat base or rounded topped columns with smooth surfaces of

uniform color. Some of the gastroscoped patients showed an unevenness and irregularity of surface that was gray or pearly white with mottling and blotches or streaks that merged the broad base pedicle with the surrounding mucosa. In these patients the rugae in the immediate area of the tumor were obliterated. There was little or no disturbance in peristalsis, nor evidence of spasm. Retention was uncommon except where the lesion was found near the pylorus. During the combined gastroscopic and roentgenologic study, the gastric pattern in 13 patients or 20 per cent was suggestive of carcinoma of the stomach.

TABLE II

FREQUENCY, AGE AND SEX DISTRIBUTION OF DIFFERENT TYPES OF BENIGN TUMORS IN 14,620 CONSECUTIVE AUTOPSIED PATIENTS
142 BENIGN TUMORS OF THE STOMACH

Tumor	No of Cases	Sex		Age	Incidence
		M	F		
Adenomatous Polyps (Single)	50	42	8	19-88	35.2
Adenomatous Polyps (Multiple)	2	0	2	40-59	1.4
Carcinoid	3	1	2	30-49	2.1
Leiomyoma	55	19	36	20-59	40.0
Lipoma	6	2	4	19-49	4.2
Fibroma	5	2	3	30-69	3.2
Inflammatory Polyps	7	4	3	40-59	5.0
Hemangioma	2	0	2	40-69	1.4
Eosinophilic Granuloma	3	1	2	30-59	2.1
Dermoids	3	2	1	20-49	2.1
Neuroma	4	2	2	30-59	2.8
Neurofibroma	2	1	1	40-69	1.4
Total	142	76	66		

The incidence of adenomatous polyps and of single lesions in in favor of males, and that of multiple lesions is in favor of females, a finding consistent with observations of other investigators.

The patients presenting small or large benign intragastric tumors a distance from the pylorus were asymptomatic. Patients with benign gastric tumor near the pylorus had gastric pain, discomfort with eructation or vomiting with little relation to food which at times made symptoms worse chiefly when the benign tumor was suspended on a pedicle on the lesser curvature near the pylorus.

Gross and Microscopic Features

Of the 65 primary adenomatous polyps from autopsied and gastrectomized patients, 62 were single and 3 multiple. Of the single group, 26 were pedunculated and 36 were sessile. Of the 3 multiple polyps, all were pedunculated. The pedunculated polyps measured 0.8 cm. in the smallest diameter and 10.7 cm. in the largest diameter. The pedicles were broad or narrow, and measured 0.9 x 0.1 cm. up to 12.3 x 0.8 cm. The sessile polyps were broad, flat or slightly raised and measured 2.5 cm. in their widest diameter. Polyps were found at the cardiac, fundus, antrum, prepyloric or pyloric region, on the anterior or posterior walls of the stomach. Regardless of the number or size of polyps, they did not appear to occur at a common anatomic site. Three of our autopsied patients showed moderate to severe degree of accordion-like type constriction of the 1st, 2nd and 3rd portions of the duodenum as a result of the telescoping of a large adenomatous polyp suspended on a long broad pedicle (Fig. 1a).

Formalin-fixed sections from the body, pedicle and base of the gastric polyps, and their adjacent gastric mucosa were studied microscopically to ascertain the character and extent of the lesion and the nature and the changes in the adjacent gastric mucosa.

All sections were stained with hematoxylin eosin and Myers' mucicarmine

All surgically resected tumors with their respective lymph nodes were examined microscopically. Multiple sections were made and the tumors were cut perpendicular to the surface, so that the base could be adequately studied. All lesions from autopsy and surgical material were submitted to the following scrutiny: nature of attachment of lesion to stomach mucosa; type of cellular infiltrate into the stalk; character of epithelium and degree of cellular variation; papillary tufting; secondary gland formation; stratification and amount of mucus secretion; presence and number of mitoses; nuclear and cellular apolarity; nuclear size, shape and staining characteristics. Care was taken to rule out low grade non-infiltrating papillary carcinoma, or microscopic foci of cytologic (*in situ*) carcinoma in an otherwise structurally benign adenomatous polyp of the stomach.

The following is a composite microscopic picture of multiple sections of the adenomatous polyps. Some presented slender finger-like projections attached to broad or narrow bases. Minor variations in structure and cells, without basic architectural alteration of mucus glands, were observed. There was little, if any, active glandular proliferative process in the smaller adenomas, and the adjacent normal mucosa was continuous over the surface of the adenoma. In the larger adenomas the glands appeared to be increased in size and number, assuming a branching pattern with their epithelium showing no departure from the normal (Figs. 3a and 3b). The surface epithelial covering appeared con-

tinuous with the glands beneath, without sharp distinction between the surface epithelium and that of the deep glands lying in the *muscularis mucosa*. This appeared as a constant finding except in occasional examples where severe diffuse inflammatory reaction resulted in active proliferation of glandular epithelium. Neither the peripheral nor central portions of the tumors showed evidence of disproportionate growth of surface epithelium that was thrown into longer projections. In occasional instances the adenomatous gland appeared to arborize from a central stalk forming multilobular compounded masses. The degree of mucus secretion varied markedly in different portions of the individual adenomatous polyps. A conspicuous pattern was that of mucus secreting glands

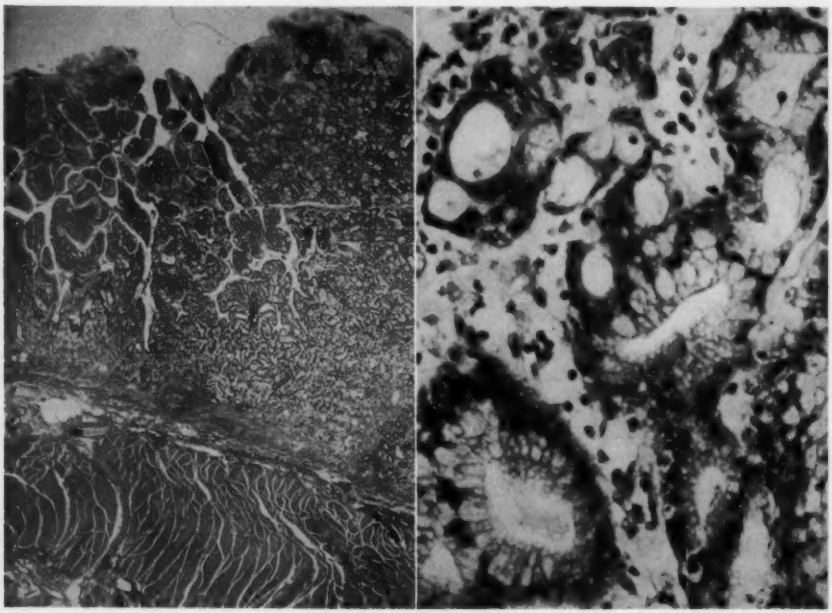

Fig. 4a Fig. 4b

Fig. 4a—Low power view of polyp showing glandular slender finger-like projections, microcysts, severe intestinal metaplasia of polyp and adjacent gastric mucosa without basic architectural alteration of mucus glands. Note the continuous surface of glandular epithelium with the glands beneath lying deep in the *muscularis mucosa*.

Fig. 4b—Higher magnification showing congestion and cellular hyperchromatism of glandular epithelium with no evidence of disproportionate growth of peripheral or central portions of the tumor.

showing dilation and transformation into microcysts. Advanced microcystic degeneration, edema, severe congestion and the associated cellular hyperchromatism were noted without distinct alteration of the glandular pattern. There was usually an extension of the submucosa and muscularis into a broad edema-

tous stalk. Interstitial inflammatory cell infiltration of the stalk in varying degree was present in all tumors. The cellular picture was that of plasma cells and lymphocytes, with a few eosinophiles and polymorphonuclear leucocytes. The adjacent mucosa, chiefly in old patients, showed conversion of the gastric pits into tubes lined by epithelial cells characteristic of the crypts of Lieberkuhn, disappearance of gastric glands, formation of microcysts, chiefly in, but not confined to the antral and pyloric mucosa. This striking change of the gastric pits is characteristic of intestinal metaplasia.

The diagnosis of "adenomatous polyp with carcinomatous transition" was based on this intestinal metaplasia in one of our surgical cases (Figs. 2a, 4a and

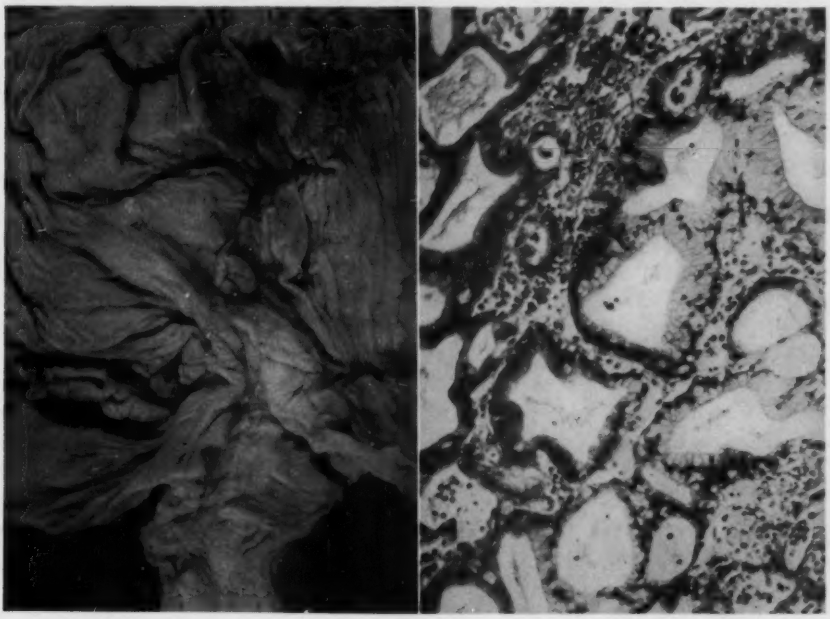

Fig. 5a Fig. 5b

Fig. 5a—Multiple pedunculated adenomatous polyps in antrum and pyloric regions of the stomach with adjacent and distant hypertrophied gastric mucosa.

Fig. 5b—Medium magnification showing severe intestinal metaplasia with diffuse inflammatory activity and microcyst formation.

4b). The patient was observed semiannually for eight years following surgery. He was autopsied and found to have: severe left ventricular myocardial infarction and pericarditis. No local or regional neoplastic process was found. Microscopic examination of the respective viscera and remaining stomach, pylorus and duodenum were without evidence of malignant disease. The origi-

nal surgical material was reviewed. The lesion was reevaluated as a benign adenomatous polyp showing intestinal metaplasia in the adjacent mucosa.

The microscopic picture of the 13 gastrectomized and 52 autopsied patients showed the periphery of the polyps in 10 gastrectomized and 19 autopsied patients to have undergone the conversion of gastric pits and disappearance of gastric glands characteristic of intestinal metaplasia. There was frequent extension of the submucosa and muscularis into the stalk which in no instance, however, showed tumor invasion. The affected areas were clearly marked off from the adjacent tissue with little or no inflammatory reaction. In two gastrectomized cases with single polyp and 23 autopsied cases, the mucous membrane away from the polyps was characterized by atrophic gastritis with reduction of gland tissue. In the remaining one gastrectomized and two autopsied cases with multiple polyps the mucosa on the drawn out pedicle and the adjacent surfaces were characterized by hypertrophic gastritis with marked inflammatory changes and intestinal metaplasia (Figs. 5a and 5b). In five autopsied cases severe interstitial chronic inflammatory activity of the stalk was present without evidence of malignant change or invasion (Figs. 6a and 6b).

Comment

The term polyp has come to imply a pedunculated tumor, especially in hollow organs. The term is indicative of a gross physical characteristic rather than any pathogenetic mechanism. Two varieties of polyps exist, namely, true adenoma and gastritis polyposa, a term coined by Meulengracht[28]. This distinction is similar to that of Muir[29], who stated that polyps may be neoplastic or inflammatory. The latter is a hypertrophic inflammatory gastritis bearing little relation to true adenoma. Hurst[17], Menetrier[20] and others[25] pointed out that inflammation produced experimentally has seldom, if ever, produced a tumor with the microscopic features of a true adenoma. Chronic gastritis, a concomitant feature in the majority of pedunculated polyps, is rarely the occasion of the growth of a true adenomatous polyp, and not then, its origin. Hurst[17] has pointed out that adenomatous polyps, like ulcers and chronic gastritis, may be looked on as precursors of carcinoma of the stomach, but rarely is such conversion proven beyond doubt.

Miller, Eliason and Wright[12,23] defended their high incidence of 35 per cent of carcinoma of the stomach arising from benign polyps. They based their findings on 24 collected and 8 personal cases of gastric polyps. They admitted, however, that in each instance the possibility existed of a carcinomatous polyp springing directly from a primary malignant process in the gastric wall.

Douglass[8], Mills[24] and Stewart[39] each report a case of gastric carcinoma with associated benign polyps. Both Douglass and Stewart believe that the carcinoma might have originated in a similar benign polyp, but Mills expressed

the opinion that this had not occurred in his case because of the distance of the malignant lesion from the benign ones and its fundamentally different structure.

Edwards and Brown[10] following their studies of 17 cases of adenomatous polyps of the stomach and five cases of carcinoma associated with benign gastric polyps, concluded that carcinomatous and benign polyps occurring in the same stomachs are in many instances uncritically regarded as examples of malignant degeneration in benign gastric polyps.

Stewart[38] and others[11,22,33] have noted many times that benign and malignant lesions are found in the same stomach, calling attention to the fact that

TABLE III

FREQUENCY, AGE AND SEX DISTRIBUTION OF DIFFERENT TYPES OF BENIGN TUMORS IN GASTRECTOMIZED PATIENTS
33 BENIGN TUMORS OF THE STOMACH

Tumor	No of Cases	Sex		Age	Incidence
		M	F		
Adenomatous Polyps (Single)	12	7	5	50-59	36.4
Adenomatous Polyps (Multiple)	1	0	1	43	3.0
Carcinoid	1	0	1	46	3.0
Leiomyoma	14	2	12	40-59	42.4
Fibroma	2	1	1	30-49	6.6
Inflammatory Polyps	2	1	1	50-59	6.6
Eosinophilic Granuloma	1	0	1	56	3.0
Total	33	11	22		

The findings in the gastrectomized patients follow the pattern seen in autopsied patients.

in such cases it cannot be shown that the carcinoma developed from a benign growth, but that from its situation it is possible.

Mills[24] collected 19 cases of gastric polyps of which four were associated with malignant growth. In three of the cases the ulcerating cancer was found with the polyp situated at a distance from it.

Paul and Logan[31] feel that the polypoid carcinomas are malignant originally, and do not arise from benign gastric polyps.

Yarnis and associates[44] reported 73 cases of gastric adenomas. In 36 gastric resection was done. Malignant degeneration of an adenoma was reported in one patient diagnosed gastroscopically and roentgenologically. The patient returned four years later with a medullary carcinoma in the same area. The

authors admitted, however, that proof of malignant degeneration arising in the adenoma was lacking.

Carey and Hay[4,5] feel that the association of malignant and benign polyps is the result of independent growth of each and does not represent malignant degeneration of the benign polyp. They have followed 30 patients with single benign polyps for periods from one to nine years and in none have they seen carcinoma develop. From their experience following critical scrutiny of 71 cases of polyps of the stomach, transition from benign to malignant status has not been demonstrated. They stated that recurrent growths seen after excision of

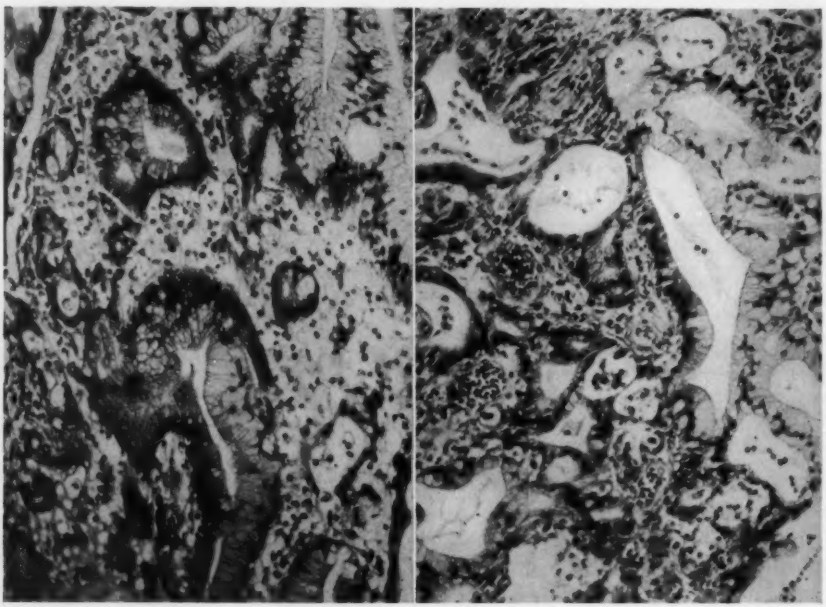

Fig. 6a Fig. 6b

Figs. 6a and 6b—Medium magnification showing intestinal metaplasia with microcystic degeneration, edema, severe congestion and cellular hyperchromatism of both adjacent and distant gastric mucosa, respectively, with severe inflammatory activity of both polyp and stalk.

benign polyps remained benign, whereas recurrences of polypoid lesions identified as cancer must have been cancer initially. Increase in the number of polyps in a particular stomach did not imply malignant tendency, and adenocarcinoma may grow independently in stomachs with single or multiple benign adenomatous polyps.

Since Menetrier's[21] introduction of the subject of intestinal metaplasia, the problem of metaplastic transition to carcinoma as it relates to adenomatous

polyps of the stomach remains unsettled. There is no question that in some instances difficulty exists in the interpretation of advanced varieties of intestinal metaplasia of the stomach mucosa. Whether to regard it as a functional transition in individuals of advanced age, or a precancerous lesion or carcinoma *in situ* can be a problem. This is particularly difficult in patients with pernicious anemia.

Such difficulty was experienced in one of our own gastrectomized examples originally diagnosed as "carcinoma", only to be proven a benign adenomatous polyp eight years following surgery, from the review of the original slides and autopsy material. This was an opportunity, we believe, rarely afforded to others, permitting final correction of the original diagnostic error in the case.

The difficulties in differentiating between intestinal metaplasia, precancerous changes and carcinoma in the course of histologic studies of the polyp, stalk and the immediate or distant gastric mucosa were related by Menetrier[21] seven decades ago. He described the irregular glandular proliferation of the epithelium with cyst formation in benign gastric adenomas, and the change of the gland elements to goblet cells producing mucus and to cells of a functionally undifferentiated character.

Menetrier's[21] basic observation and conclusions on intestinal metaplasia set in motion investigations by Hari[16], and Clar[7] who regarded such transition as a congenital abnormality. Magnus[19], Schindler[36], Stout[41], Warren and Meissner[42] regarded it as a faulty degeneration of the surface epithelium in a mucosa repeatedly damaged by gastritis, or as a metaplasia resulting from chronic irritation.

Attempts by some investigators[26,27] to attach significance to intestinal metaplasia as a "precancerous" progression, by others as "carcinomatous" become questionable in the face of admission of failure to demonstrate the transition from intestinal metaplasia to carcinoma. We believe that failure by some investigators to designate "age" as a most common contributor to incidence and extent of metaplasia as indicated by Geissendorfer[15] and Faber[13,14], affects the conclusion in a given case when intestinal metaplasia and carcinoma are associated. Even in pernicious anemia[35] with its very high incidence of gastric carcinoma, it seems advisable to regard other factors as important in the carcinogenesis rather than to consider the ever present severe intestinal metaplasia as the basic "cause".

Summary

We have presented 65 cases of benign gastric polyps from the autopsy and surgical files of Metropolitan, Flower and Fifth Avenue Hospitals. These patients were under study for periods of 19 months to 23 years and not one of them showed malignant change of the polyp. In one instance intestinal meta-

plasia was temporarily but erroneously considered to represent cancerous degeneration.

The pertinent literature referable to polypi and their possible relationship to gastric cancer has been reviewed. While agreement on this point is lacking, it is evident that malignant degeneration of a benign polyp must be a very rare occurrence and uncontested proof of such transformation seems to be lacking. It has also been shown that intestinal metaplasia in or adjacent to polyps is not sufficient histological evidence of precancerous change, carcinoma *in situ* or of malignant degeneration.

Our studies further indicate that benign polyps in themselves are rare. They may be asymptomatic or interfere with the movement of the stomach, especially when situated at the pylorus. They are of clinical importance because of the uncertainty of the lesion and a source of hemorrhage leading to hypochromic anemia. They may produce pyloric obstruction, rarely showing degrees of accordion-like constriction terminating in infarction and gangrene of both tumor and bowel.

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President's Message

Oaks From Acorns Grow

The report of the Nominating Committee will be sent to all Fellows of the American College of Gastroenterology no later than two months before the annual convention. The nominating committee is appointed by your President according to our By-Laws. It is composed of two Trustees, two Governors, and a Fellow-at-large. They nominate candidates for all of the elective offices. Additional nominations may be made by the signed endorsement of fifteen Fellows or life Fellows entitled to vote. The additional nominations shall be added to the list of nominees, by the secretary, at least thirty days before the annual meeting. An attempt is made to give all areas fair representation in order to promote stability and a healthy growth of our organization.

Appointments of Committees are made by the Board of Trustees. In the past some Fellows have expressed disappointment because they could do no better than receive an appointment to a Committee.

In my opinion Committee appointments are among the most important offices of our organization. At the Committee level the neophyte has his opportunity for constructive action. His thinking can be evaluated and his judgment can be studied. He has the opportunity to express his creative abilities. His real personality can be demonstrated at all levels of discussion. Defects of character and personality not consistent with good leadership can be assessed during the long, hard effort that goes with effective Committee work.

Leadership qualities are discovered, and with all things equal a Committeeman can become Chairman. He then becomes eligible for his nomination as Fourth Vice-President. Certainly one can say the Committee is the acorn from which great oaks grow.

Arthur A. Kirchner

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GASTROINTESTINAL TRACT

PANEL DISCUSSION ON THE COMPLICATIONS OF PEPTIC ULCER: INTRACTABLE PEPTIC ULCER: Addison G. Brenizer, Jr. North Carolina M. J., 17:211 (May), 1956.

A peptic ulcer is called intractable when medical treatment has failed. Failure is decided upon when a patient has to be hospitalized a number of times a year, or when he loses a great deal of time away from his occupation because of his ailment. Ulcers that give constant pain not relieved by food or alkali and those that cause loss of sleep, repeated episodes of bleeding or partial obstruction, are considered intractable and should be referred to the surgeon. Intractability is common in cases of severe hyperacidity, hypersecretion, multiple ulcers, and in ulcers that lie in the second part of the duodenum. Ulcers which lie on or adjacent to the pyloric sphincter are also oft times refractory to medical treatment. One must, however, not rush off to surgery, cases which are refractory because of personality factors. Traveling salesmen, truck drivers, school teachers and night workers are notoriously difficult patients to manage. Drug addicts and psychoneurotics particularly, should be spared the knife. Partial or subtotal gastrectomy is the treatment of choice in those patients requiring surgery.

A. J. BRENNER

CORROSIVE (ACID) GASTRITIS: MANAGEMENT OF EARLY AND LATE CASES: Frederick Steigmann and Robert A. Dolehide. New England J. Med., 254:981 (24 May), 1956.

The entity of corrosive (acid) gastritis has received little attention in the American literature, and the concept of the management of such cases is somewhat nebulous, as few patients survive the initial insult for more than 24 hours. It is not common knowledge that caustic alkalis exert their liquefaction necrosis primarily on the oral and esophageal mucosa, with usually little if any effect on the gastric mucosa because of the neutralizing action of the stomach secretions. Acids, in contrast, are notorious for their coagulation necrosis of the gastric mucosa with acute and chronic sequelae. The acute symptoms may include hemorrhage, shock and "perforation" with peri-

tonitis. The late sequelae may be classified according to the amount of destruction and the resultant scar formation: pyloric stenosis, antral stenosis, hour-glass deformity or rarely total gastric scarring resulting in a linitis plastica. The obstructive symptoms can begin anywhere from a few weeks to years, with an average of four to six weeks, after the acute phase of corrosive poisoning has subsided. The treatment of the acute stage is supportive-medical. The treatment of the sequelae is surgical—pyloroplasty or gastroenterostomy, depending on the findings at laparotomy. Subtotal gastric resection is rarely indicated.

ARNOLD L. BERGER

GASTRIC DISTENTION FROM INGESTED AIR: Lothal Wirth. Military Med., 118:577 (June), 1956.

The author points out that in some individuals the phenomenon of "air sucking" is present. He has observed two cases in which it was possible for air to enter the stomach directly, without the mechanism of swallowing. He suggests the use of a suction apparatus as a means of control if gastric distention results.

JOHN N. DILL

HEMORRHAGIC THROMBOCYTHEMIA: Theodore H. Spaet, Stephen Bauer and Samuel Melamed. Arch. Int. Med., 98:377, 1956.

A 71-year old female was suffering from recurrent attacks of massive gastrointestinal hemorrhage, especially melena. No other symptoms of bleeding tendency were encountered except one spell of epistaxis. Hematological examination revealed an enormous increase of platelets (10 millions per cubic mm.) The blood marrow was studded with megacaryocytes. The red cell picture alternated between microcytic anemia and polycythemia depending on the amount of bleeding. After prolonged observation the diagnosis of polycythemia vera was made with thrombophilia, the latter being responsible for the bleeding diathesis. It was shown that a moderate increase of platelets causes a clotting tendency, while a great increase interferes with the thromboplastin regeneration and produces bleeding. This case demonstrates the diagnostic problems of melena, especially as the patient has an old deformity of the bulb, but no sign of active ulcer disease.

H. B. EISENSTADT

STUDIES ON THE TEMPERATURE OF THE GASTROINTESTINAL TRACT: Shigeaki Katsura. Tohoku J. Exper. Med., 64:27 (25 June), 1956.

The temperature changes in the esophagus, stomach and duodenum of healthy adults were studied after drinking water at 15° and 50°C. The following facts were confirmed: 1. The upper alimentary tract acts as a buffer to the temperature of ingested fluid. 2. The temperature change in the esophagus shows the maximum variation and is always greater than the temperature change in the stomach. 3. The temperature change in the stomach shows the next greatest variation, with the upper and lower portions of the stomach behaving equally. 4. The temperature change in the duodenum shows the smallest variation and never exceeds that found in the stomach.

ARNOLD STANTON

CHANGING CONCEPTS AND PRACTICES IN THE APPROACH TO DISEASES OF THE DIGESTIVE TRACT: Chester M. Jones. New England J. Med., 254:1197 (28 June), 1956.

The author suggests further study of the nutritional problems and occasional troublesome diarrhea that follows radical resection and anastomotic operations. Careful stool culture in some of these cases has shown unsuspected presence of salmonella, which may well have been responsible for increased bowel activity. It is suggested that possibly the loss of gastric acidity as a protective mechanism against ingested bacteria may be the cause of some of these troublesome symptoms.

JOHN E. COX

STOMACH

THE OUTLOOK FOR INCREASED SALVAGE IN GASTRIC CANCER: Thomas J. Anglem. Rhode Island M. J., 39:315 (June), 1956.

According to the author, the early symptoms of gastric cancer are not well known and in his opinion, too many physicians are entirely too willing to treat patients for months without the benefit of diagnostic studies. His symptomatology is divided into three parts: one group of these patients complain of indigestion or dyspepsia, the second group, tiredness, fatigability or weakness and the third group have symptoms of peptic ulcer. Mass screening methods are of no great value. The differential diagnosis between benign and malignant gastric ulcer is difficult to determine.

Operative mortality rates are now diminished in the neighborhood of 5 to 7 per cent according to the author, as against 18 to 20 per cent which it was a few years ago. This gain of approximately 10 per cent is the patients who now have an increased chance of survival.

In essence, this is a plea for earlier recognition, surgery and less temporizing with this condition.

IRVIN DEUTSCH

GASTRIC ULCER AND GASTRIC CANCER: Martin L. Tracey. Rhode Island M. J., 39:318 (June), 1956.

According to the author, any patient with epigastric distress or discomfort of any sort who is over 40, should be fully studied and patients with indigestion that persists for three or four weeks and are not relieved by simple measures should be fully studied at all ages. He favors the use of both gastroscopy and x-ray. Once the diagnosis of benign gastric ulcer is made, every effort should be made to heal it quickly and to keep it healed. In his opinion, healing should be judged gastroscopically as well as by x-ray. Once lesions have healed, the check-up examinations should be done frequently, four times per year for the first year and twice per year thereafter. X-ray examinations should include mucosal relief and compression as well as the usual studies.

IRVIN DEUTSCH

DUODENAL ULCER: END RESULTS IN VAGOTOMIZED PATIENTS: Benjamin Goldman and James L. Schuster. J. Internat. Coll. Surgeons, 25:698 (June), 1956.

The authors give a resume of various publications reporting the results of vagotomy since its introduction by Dragstedt and Owen in 1943. They add a series of 36 of their own patients. Vagotomy should be performed only in patients with intractable ulcers or with complications such as obstruction, hemorrhage, perforation, or penetration. The postoperative management requires intubation and parenteral feeding until the gastrointestinal function has been well re-established. This should be discussed with the patient prior to the operation. The value of vagotomy in anastomotic ulcers is generally agreed upon. The same procedure seems to be preferable in postbulbar and deeply penetrating duodenal ulcers where a secure closure of the duodenal stump cannot be obtained during gastric resection. The same method seems to be preferable also in poor risk and old patients.

H. B. EISENSTADT

RECENT IDEAS IN GASTRIC SURGERY: T. H. Somervell. J. Internat. Coll. Surgeons, 25:713 (June), 1956.

Duodenal ulcer disease depends on gastric hypersecretion, the latter is mainly the result of both vagal and hormonal (gastrin) stimulation. Fasting hyperacidity is caused by vagal activity and must be differentiated from postprandial hyperacidity resulting from hormone activity. While vagotomy eliminates the nervous phase of gastric stimulation, the hormonal phase can be removed 1. by resection of the pyloric end containing gastrin, 2. by excision of the acid-secreting glands, 3. by ligation of blood

vessels that carry the hormone from the antrum to the parietal cells. These three procedures are best carried out by a resection of the lower half of the stomach, they do not require subtotal removal of this organ. The latter is a mutilating procedure especially in consideration of the small size and the extragastric location of the duodenal ulcer. Vagotomy with gastroenterostomy is sufficient in patients with duodenal ulcers who have mainly fasting hypersecretion. Hemigastrectomy is the method of choice in patients showing mainly postprandial hypersecretion. Vagotomy plus hemigastrectomy must be used if both the fasting as well as the postprandial secretion is high. The latter procedure is necessary in the majority of the cases.

H. B. EISENSTADT

INTESTINES

SURGICAL ASPECTS OF ULCERATIVE COLITIS: William S. Carpenter. J. Michigan M. Soc. 55:433 (Apr.), 1956.

The author states that in selected cases of chronic ulcerative colitis, in which medical treatment fails to control the disease, surgical intervention will effect a cure. Ileostomy and colectomy in a single stage is the procedure of choice; and, again in selected cases, abdominoperineal resection may be combined with the above procedure at the same operation. The most common symptom leading to surgery is chronic uncontrollable disease, fulminating disease less commonly, and questionable perforation or massive hemorrhage only on rare occasion. The relatively frequent occurrence of malignancy in chronic ulcerative colitis makes earlier surgical intervention even more desirable. Complications due to ileostomy are of less concern than previously and technical problems are being fairly well solved. These patients seem to do well from a nutritional standpoint, and with proper handling of the ileostomy they are economically rehabilitated.

CHESTER S. SVIGALS

CLINICAL CONFERENCE ON ULCERATIVE COLITIS: Paul S. Rhoads, Jonathan Burton, Joseph C. Sherrick, Robert Brown and Walter G. Maddock. Quart. Bull. Northwestern Univ. M. School 30:21 (Spring), 1956.

This is the report of a case illustrating the natural history of chronic nonspecific ulcerative colitis. It is presented as a Grand Round case and is discussed by the departments of internal medicine, radiology, surgery, and pathology. The case combines many features of clinical interest and problems of management. *Pyoderma gangrenosum*, fluid and electrolyte disturbance producing a shock-like state, and development of pseudopolyposis are among the clinical features discussed. Laboratory data, sigmoidoscopic, and roentgenologic findings are among the diagnostic features discussed. Steroid therapy and eventually surgical intervention are among the features of management discussed. The pathologist discussed the differential diagnosis of the specific colitides and regional enteritis as well as the histopathological features of the resected colon in this particular case. The case is an interesting, though not too unusual one, and is well presented, discussed, and illustrated.

CHESTER S. SVIGALS

PAIN OF ANORECTAL ORIGIN: Wilford L. Cooper. J. Internat. Coll. Surgeons 25:524 (Apr.), 1956.

The author stresses the importance of pain as an indication of disease. He then discusses the various types of pain and their nerve pathways through which pain is transmitted from the anorectal region.

Types of pain are cutaneous or superficial—such as burning, pricking, lancinating, cutting or sharp and can be easily localized. Visceral or deep—dull, aching and induces depression and inactivity and is fairly prolonged.

Perception of pain is physiologic and de-

pends upon intactness of nerve connections and conductive pathways. Reaction to pain is basically psychogenic, highly individual and modified by complex functions.

Reaction to pain varies widely in different persons and in the same person. Objective manifestations may be affected by degree of mental anguish and discomfort. It is also influenced by environmental and familial backgrounds and emotional experiences in childhood and adult life.

There is a well-developed subepithelial nerve network in the skin of the anal canal. This is composed of fine fibres with small interspaces as contrasted elsewhere. Investigation has shown that the epithelial plexus of the nerves of the anal skin is continuous with that of the rectal mucosa. The external sphincter muscle has a double nerve supply, the first being from the medullated nerves of the sacral and coccygeal nerve root, and the second from the nonmedullated nerves of the Auerbach plexus of the vegetative system. Cutaneous pain below the pectineate line and pain arising in the external sphincter muscle is conducted by the (pudendic) spinal nerve.

The rectum and colon receives innervation from the autonomic system. For most of the descending colon pain fibres run with the sympathetic system. At the rectosigmoid junction, the innervation changes and arises from the *nervi erigenti*, pelvic splanchnic nerves and visceral branches of the sacral nerves.

LOUIS K. MORGANSTEIN

APPENDECTOMY VERSUS HEMICOLECTOMY FOR THE COLONIC TYPE OF CARCINOMA OF THE APPENDIX: Willard J. Kiser, Laurel G. Case, Leo P. Cawley and Bert E. Stofer. J. Internat. Coll. Surgeons 25:566 (May), 1956.

A review of 31 cases of colonic type carcinoma of the appendix indicates that where infiltration is beyond the mucosa, (Stage II), the operation of choice should be hemicolectomy; simple appendectomy results in 16.7 per cent recurrence.

Simple appendectomy in 13 out of 14 cases of Stage I category, resulted in one case of recurrence.

In 14 cases of Stage II classification, 7 had simple appendectomies with 1 dead less than five years postoperatively, 1 living with recurrence, 4 living free of disease, 1 postoperative death. The other 7 had hemicolectomy as standard procedure with 1 dead two years postoperatively, 6 living and well, 2 to 14 years postoperatively.

These figures seem to indicate that when diagnosis of this rather uncommon neoplastic disease is made, the more radical hemicolectomy is indicated, even in the early Stage I classification.

J. EDWARD BROWN

INTESTINAL OBSTRUCTION: REPORT ON 12,614 CASES IN JAPAN: Kiyoshi Saito. J. Internat. Coll. Surgeons 25:541 (May), 1956.

Records of 175 hospitals in Japan over a number of years, indicate a high incidence of mechanical intestinal obstruction, with operative interference in 92 per cent of the cases and a mortality of 23 per cent.

Simple kinking occurred in 33 to 40 per cent of the studied cases, 12 per cent were due to adhesion bands, 10 per cent volvulus, 18 per cent tuberculosis, 18 per cent intussusception.

Postoperative adhesions in 1935 accounted for 10 per cent of all obstructions, but in 1955 was responsible for 30 per cent of all operated cases, and the bulk of these fell into the kinking category.

Fifty per cent of postoperative adhesions followed simple appendectomy, (the author chides his fellow workers with "once surgeons' hands enter the peritoneal cavity adhesions are to be expected").

J. EDWARD BROWN

EXPLORATORY LAPAROTOMY TO RULE OUT MALIGNANCY: T. B. Hubbard and T. B. Hubbard, Jr. J.M.A. Alabama 25:299 (June), 1956.

The authors have been impressed with a number of cases who have been extensively investigated for malignant disease and declared sound six months to a year before x-rays finally showed larger and more extensive lesions. They present several case

reports to suggest that a more aggressive philosophy should be adopted based upon the fact that x-rays are not infallible and an exploratory laparotomy today carries very little risk. It is suggested that in a patient over 40 years of age, who develops for the first time persistent abdominal pain of unknown etiology, diagnostic investigation is not complete until laparotomy has been performed.

JOHN M. MCMAHON

COMBINED BACILLARY AND AMEBIC ULCERATIVE COLITIS ASSOCIATED WITH ATYPICAL PNEUMONITIS AND SHIGELLA-POSITIVE SPUTUM: Edward C. Raffensperger. Am. J. Med. 20:964 (June), 1956.

A case of combined bacillary and amebic dysentery occurred in a 59-year old Negro apparently with a prolonged blood stream infection. The disease persisted for several months and appeared at first as purulent bronchopneumonia with Sonne bacillus in the sputum. The pulmonary episode lasted one month and was followed by a latent period of several months after which an acute dysentery with bloody diarrhea occurred where the same bacillus was recovered from the stool. In addition to the bowel ulcerations, however, a mass could be felt in the rectum which proved to be an amebic granuloma on biopsy.

H. B. EISENSTADT

ACUTE HEMORRHAGIC ENTEROCOLITIS: Alton M. Paull. Rhode Island M. J. 39: 320 (June), 1956.

This case is one of a middle-aged man with chronic heart disease and diabetes mellitus who had a sudden onset of a bloody diarrhea. The findings simulated those of an acute mesenteric thrombosis but this case went on to exitus and was posted, at which time, an acute hemorrhagic enterocolitis was found. It is suggested that cellular anoxia is the most important factor in the pathogenesis of this disease. Unnecessary surgery should not be undertaken in this condition.

IRVIN DEUTSCH

BIOPSY STUDIES IN ULCERATIVE COLITIS: S. C. Truelove and W. C. D. Richards. Brit. M. J. 4979:1315 (9 June), 1956.

Small biopsy specimens of the colonic mucosa from just above the rectosigmoid junction have been obtained in 111 instances from 42 patients with ulcerative colitis. A group of 24 patients not suffering from ulcerative colitis and with apparently normal mucosa at sigmoidoscopy have been similarly studied as a control group. Specimens obtained from the control group were all normal apart from two which showed slight histological changes.

Among 71 specimens from patients with ulcerative colitis in the stage of symptoms, 67 showed inflammation. More than half of the 40 specimens taken from ulcerative colitis patients in clinical remission showed inflammation. Brief details are given of two patients being studied by serial biopsy in whom histological relapse preceded clinical relapse by some weeks.

ARNOLD L. BERGER

ABNORMAL EPITHELIAL CELLS IN ULCERATIVE COLITIS: M. M. Boddington and S. C. Truelove. Brit. M. J. 4979:1318 (9 June), 1956.

Examination of the colonic epithelial cells has been facilitated by use of an instrument utilizing a special "perspex" head. Examination by Papanicolaou's method has revealed that abnormal cells are often present in ulcerative colitis.

In their most pronounced form, the abnormal cells are much enlarged and possess large nuclei with prominent nucleoli and a disturbed chromatin pattern. These abnormal cells may be found in any patient with abnormal sigmoidoscopic findings, but are most frequent in patients with severe disease. They are commonly found in patients in their first attack of ulcerative colitis.

There seem to be three possible explana-

tions for the occurrence of these cells: 1. they are to be expected whenever the colonic epithelium is provoked into vigorous regenerative activity by extensive damage from whatever cause; 2. they represent a primary epithelial disturbance in ulcerative colitis, as for example, a maturation arrest due to the absence of a specific factor necessary for epithelial development; 3. they are abnormal cells secondary to severe inflammation in the colonic mucosa.

The abnormal cells have many of the features of malignant cells, a point of interest in view of the fact that patients with ulcerative colitis are unduly liable to develop carcinoma of the colon.

ARNOLD L. BERGER

LIVER AND BILIARY TRACT

SURGERY OF THE BILIARY TRACT: PART I: Marshall K. Bartlett and William C. Quinby, Jr. New England J. Med. 254:154 (26 Jan.), 1956.

This article evaluates the experience with cholecystectomy and choledochostomy at the Massachusetts General Hospital covering the eleven years from 1943-1953 with particular reference to the mortality and complications. There were 2,243 operations for chronic cholecystitis. Ninety per cent of these cases had stones in some part of the biliary tree. Forty-three per cent of these cases had an exploration of the common duct and in 38 per cent of these cases stones were found. Thus 16 per cent of these cases had stones removed from the common duct.

Cholecystectomy was done in 1,280 cases with a mortality of 0.6 per cent (8 deaths). Only one of these deaths was directly related to the operation. There were 113 nonfatal complications. One-half of these were directly related to the operative procedure with wound sepsis heading the list.

Choledochostomy in addition to cholecystectomy was done in 963 cases with a mortality of 1.8 per cent (17 deaths). One-half of these deaths were directly related to the operation. There was no significant difference in the operative mortality in cases with and those without stones found in the common duct. None fatal complications occurred in 94 cases or 9.8 per cent. Here again wound complications, especially wound sepsis, played an important part.

Deaths directly attributable to the operative procedure predominated in patients with common duct stone, whereas deaths due to general hazards of major abdominal surgery were more common in patients with negative common duct exploration.

To reduce the death rate, operation should be done earlier in the course of the disease, before indications for common duct exploration have had time to occur. Operations should also be done earlier in the life of the patient.

Reappraisal of the indications for common duct exploration is in order since only half of the ducts explored contain stones and the necessity for secondary operations for overlooked stones are very infrequent.

Sufficient accuracy in operative cholangiography has not as yet been obtained to significantly effect the mortality. However, further improvement in the technic of common duct explorations must be sought since a substantial number of deaths were due to pancreatitis, bile peritonitis, sepsis, all related to the operative procedures.

ALEXANDER ZABIN

SURGERY OF THE BILIARY TRACT: PART II: Marshall K. Bartlett, William C. Quinby, Jr. and Gordon A. Donaldson. New England J. Med. 254:200 (2 Feb.), 1956.

This paper evaluates the concepts and methods of treatment in 716 cases of acute cholecystitis seen at the Massachusetts General Hospital 1943-1953. Comparison is also made with mortality and morbidity figures of the treatment of the chronic or interval phase of the disease.

In this series of 716 cases, there were 21 deaths, a mortality of 3.0 per cent; 124 cases were treated without operation, 37 with cholecystostomy, 401 cases with cholecystectomy and 154 cases with cholecystectomy and choledochostomy.

In the 401 patients treated by cholecystectomy there were five deaths, a mortality of 1.2 per cent. In the chronic group the mortality was .6 per cent. There were 38 nonfatal complications, a rate of 9.6 per

cent. In the chronic group this was 8.9 per cent. Wound sepsis was the commonest complication. Biliary peritonitis occurred 3 times, necessitating reoperation in each instance.

There were 154 patients who had common duct exploration at the time of cholecystectomy for acute cholecystitis, a rate of 26 per cent. In the chronic group this amounted to 43 per cent. Forty-three per cent of the ducts explored contained stones, as opposed to 38 per cent in the chronic group. There were six deaths, a mortality rate of 3.9 per cent. In the chronic group the rate was 1.8 per cent. There were 19 nonfatal complications or a rate of 12.8 per cent, as compared to 9.8 per cent in the chronic group. Since choledochostomy adds considerably to the operative risk and since more than one-half of the ducts explored did not contain stones, it seems that continued efforts to improve indications for and technic of choledochostomy should be made.

ALEXANDER ZABIN

AN EVALUATION OF EARLY OPERATION IN ACUTE INFLAMMATION OF THE GALLBLADDER: Patrick C. Shea, Jr. J.M.A. Georgia 45:41 (Feb.), 1956.

This paper reviews 209 consecutive cholecystectomies, performed over a 3-year period and operated on by the resident housestaff. It concerns only the nonmalignant inflammatory diseases of the gallbladder, either acute, chronic or both. Fifty-one of the patients were operated on within 24 hours after admission, the remaining 158 were selected for cholecystectomy at a later date.

Early operation was indicated when progressive rebound tenderness, continued or heightened fever, persistent elevated white count, and constant or increasingly severe pains were present.

The mortality was low: 6 cases died and all of them would have been probable mortality cases without the operation. The percentage of mortality in early operations was 5.9, and 15.8 with exploration of the common duct. The mortality rate increased with the age above 50. Complications occurred in 14 per cent of the elective group and in 37 per cent in the group operated on within 24 hours of admission. The paper gives a good review of how acute gallbladder cases should be treated and will find the agreement of many surgeons and physicians.

HELMUTH NATHAN

THE SURGICAL TREATMENT OF BILIARY DYSKNESIA: Wyatt C. Simpson. J.M.A. Alabama 25:180-182 (Feb.), 1956.

The author reports three patients with biliary dyskinesia who are treated surgically by transduodenal section of the sphincter of Oddi. One patient was completely relieved, another was considerably improved and the third still had attacks of colic similar to those experienced before this procedure, although less frequent and less severe. The author feels that the operation is not a panacea for biliary dyskinesia but is definitely worth trying. Technically, it is less difficult and less hazardous than choledochoduodenostomy and should be tried in suitable cases before a more radical procedure is adopted. Unfavorable results may be avoided by adopting a technic recommended by Jones and Smith whereby a wedge is taken out of the sphincter and duodenal and common duct walls and the mucosa united by interrupted sutures.

JOHN M. MCMAHON

ELECTROCARDIOGRAPHIC AND BLOOD-PRESSURE CHANGES DURING AND AFTER BILIARY TRACT SURGERY: David Mendelsohn, Jr. and Richard Monheit. New England J. Med. 254:307 (16 Feb.), 1956.

The authors made extensive studies in an attempt to shed some light on the time-honored relationship between biliary tract pathology and the heart. Although they were not able to explain the physiodynamics of this relationship they have arrived at certain conclusions which deserve recording. They concluded that the frequency of silent postoperative myocardial infarction in their series of biliary tract surgery suggests that

routine preoperative and postoperative electrocardiograms should be taken on cardiac patients undergoing major surgery. In their series reflexes arising from the biliary tract during surgery were not clinically significant except in one case. They also noted that there are few arrhythmias and conduction disturbances under thiopental, nitrous oxide and succinylcholine chloride anesthesia.

BERNARD J. FICARRA

OCCLUSIVE HEPATIC VENOUS CATHETERIZATION IN THE STUDY OF THE NORMAL LIVER, CIRRHOSIS OF THE LIVER AND NONCIRRHOTIC PORTAL HYPERTENSION: W. J. Taylor and J. D. Meyers. Circulation 13:368 (Mar.), 1956.

The technic of occlusive venous catheterization of the liver in man is described. The pressure obtained in an occluded small hepatic vein has been termed the wedged hepatic venous pressure. In cats, the wedged hepatic venous pressure and portal venous pressure are essentially the same.

In 29 observations on 27 patients with Laennec's cirrhosis, the wedged hepatic venous pressure has, in each instance, been higher than any observation in 18 control subjects, thus establishing diagnostic significance for an elevated pressure. The procedure has been of practical value in the separation of cirrhotic from noncirrhotic (extrahepatic) portal hypertension. The wedged hepatic venous pressure is particularly high in those cirrhotic subjects with esophageal varices and with jaundice, but the degree of elevation cannot be correlated with the presence or absence of ascites.

ARNOLD L. BERGER

BILIARY TRACT STUDIES I—X-RAY DIFFRACTION ANALYSIS OF GALLSTONES; CORRELATION WITH OCCURRENCE OF MICROSPHEROLITHS IN BILE: K. Junpeir, Jr. and William E. Woolf. Am. J. Med. 20:383 (Mar.), 1956.

The authors report the results of a correlative study of the minute particulate content of bile and gallstones, employing microscopic examination and x-ray diffraction analysis. Microspheroliths found in bile or gallstone fragments in 23 of the 200 patients studied are described. Microscopic examination of bile and gallstone fragments together with the x-ray diffraction studies of gallstones indicates that some of these microspheroliths contain calcium, usually in the form of calcium carbonate. Data presented indicates that increased calcium concentration in gallbladder bile, increased pigment excretion in hepatic bile and unknown changes in hepatic bile composition probably are responsible for the microspherolith formation. The presence of such crystals and duodenal drainage bile suggests the presence of calcium containing gallstones. The possibility of a hemolytic anemia should be considered if large numbers of pigmented microspheroliths are found.

JOHN M. MCMAHON

INTRAHEPATIC AND EXTRAHEPATIC PORTAL VENOUS THROMBOSIS: Waldyr da Silva Prado and Jose Luiz Camargo Barbosa. J. Internat. Coll. Surgeons 25:306 (Mar.), 1956.

A case is reported of portal hypertension with chronic splenomegaly in which, after intensive preoperative therapy, the patient was splenectomized. Twenty days after the operation hematemeses began which recurred daily with increased frequency and severity. In spite of all efforts to control bleeding, the patient died two months after the operation.

At autopsy, thrombosis of the portal and mesenteric veins was present. In addition to intrahepatic venous thrombosis, diffused hepatic stenosis was present, as were esophageal varices.

Inasmuch as this patient was from a region highly infested by *S. mansoni*, the authors are of the opinion that the giant splenomegaly in this case had schistosomatic origin. The patient was a Bahian farmer who was accustomed to bathing in neighboring lakes. (This first suggested the possibility of schistosomiasis).

JOHN E. COX

OCCLUSIVE HEPATIC VENOUS CATHETERIZATION IN THE STUDY OF THE NORMAL LIVER, CIRRHOSIS OF THE LIVER AND NONCIRRHOTIC PORTAL HYPERTENSION: W. Jape Taylor and J. D. Myers. Circulation 13:368 (Mar), 1956.

The technic of occlusive venous catheterization of the liver is described. The pressure obtained in an occluded small hepatic vein has been termed the wedged hepatic venous pressure. In cats, the wedged hepatic venous pressure and portal venous pressure are essentially the same.

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ARNOLD L. BERGER

POSTHEPATITIS CIRRHOSIS: Stuart G. McAlpine. Scottish M. J. 1:217 (June), 1956.

The author studied 20 patients of infective hepatitis who later developed posthepatitis cirrhosis. He is of the opinion that there is some clinical evidence that inadequate medical treatment, although inconclusive, may be a factor in the development of posthepatitis cirrhosis.

It is pointed out that the cirrhosis is noted only in a small number of cases following infectious hepatitis, and suggests that orthodox treatment plays a part in preventing subsequent liver damage. The author describes the usual medical management of his cases. He believes that even the mildest case of infectious hepatitis should be treated conservatively with bed rest, light diet, supplemented with glucose, until bile and urobilinogen disappear from the urine.

ZACH R. MORGAN

RELATIONSHIP OF PORTAL HYPERTENSION TO ASCITES IN LAENNEC'S CIRRHOSIS: W. J. Eisenmenger and William F. Nichol. Am. J. Med. 20:879 (June), 1956.

The authors studied the effect of portacaval anastomosis on the fluid and electrolyte balance of five selected patients with cirrhosis and chronic ascites. In these persons, ascites disappeared following the shunt operation although peripheral edema developed in several cases. These observations were presented in support of the importance of the role of portal hypertension in the formation of ascites in this condition. Although portacaval anastomosis may be beneficial in some patients it is not advocated as a general method of treating chronic ascites. In two additional patients, ascites made its first appearance shortly after portacaval anastomosis was established. The authors feel that one is probably dealing with a mechanism of ascites production which differs from that accounting for the chronic formation of ascites in Laennec's cirrhosis.

JOHN M. MCMAHON

PORTAL HYPERTENSION DUE TO CHRONIC OCCLUSION OF THE EXTRAHEPATIC PORTION OF THE PORTAL VEIN: ITS RELATION TO ASCITES: Archie H. Baggenstoss and Eric E. Wollaeger Am. J. Med. 21:16 (July), 1956.

Fifteen cases of chronic occlusion of the portal vein not complicated by other lesions that could produce ascites by themselves, such as congestive heart failure, myxedema, peritoneal carcinomatosis or tuberculosis, chronic glomerulonephritis, cirrhosis of the liver, Meig's syndrome, mediastinal vena cava compression showed clinical and pathological evidence of portal hypertension. Only in 5 of them was this disorder associated with ascites. In the group without ascites, the mean age was lower, the accessory portal veins were patent and better developed, the enlargement of the spleen and the atrophy of the liver were less marked. The result of this study emphasizes portal hypertension *per se* as an important contributing factor in the pathogenesis of ascites even in the absence of liver pathology.

H. B. EISENSTADT

PANCREAS

PANCREAS IN ALCOHOLIC CIRRHOSIS: G. Moretti, A. Geyer and M. Ducloux. La Presse Medicale 64:376 (Feb.), 1956.

The authors had previously studied the parotid glands in cirrhosis, then the pancreas in the syndrome of denutrition following gastrectomy.

The purpose of the present paper is to study the pancreas in cirrhosis from the biological and histochemical point of view. Thus is it possible to set up a dynamic picture of this gland.

There is early and constant involvement of the external pancreas. To the fall of pancreatic trypsine, lipase and amylase do correspond, in addition to trivial changes in the connective tissue, the presence of pyknosis and atrophic degeneration of a certain number of the ergastoplasm, an absence or a marked diminution of the secreting grains.

The authors discuss the significance of this histiopathology.

PANCREATIC CALCIFICATION: Luther G. Bell, Larry J. Hines and Wilton A. Doane. U. S. Armed Forces M. J. 7:348 (Mar.), 1956.

Chronic pancreatic calcification is the end stage of a serious and debilitating malady. Precipitating factors are variable but alcoholism is common. The complication of diabetes, steatorrhea, chronic malnutrition, and drug addiction are frequent. Tuberculosis, cirrhosis of the liver, and disease of the stomach and duodenum are commonly associated and add to the burden of treatment.

The clinical diagnosis of pancreatic calcification is often missed, only to be made at laparotomy or autopsy. The significance of hyperparathyroidism with pancreatic calcification is not clear but the condition suggests the study of calcium and phosphorus metabolism is more important in this disease.

The direct surgical approach is usually the treatment of choice and should be practiced in most cases as soon as the diagnosis of chronic relapsing pancreatitis is established. Total pancreatectomy is an operation of major proportions with a high mortality and should be reserved for patients in whom other attempts have failed.

ARNOLD L. BERGER

EXOCRINE PANCREATIC SECRETION. EFFECTS OF PANCREATIC DISEASE: David A. Dreiling and Henry D. Janowitz. Am. J. Med. 21:98 (July), 1956.

Pancreatic juice consists of water, electrolytes, digestive enzymes. Its flow is regulated by a hormone secreted in the upper small bowel called "secretin". Crude secretin has been fractionated into five component hormones: 1. secretin proper inhibiting increased flow of water and bicarbonates, 2. pancreozymin stimulating enzyme excretion, 3. hepatocrinin causing biliary flow, 4. cholecystokinin inducing contraction and emptying of the gallbladder, and 5. enterocrinin stimulating *succus entericus* production. In addition, intake of carbohydrates stimulates the pancreatic secretion slightly, of protein and fat greatly. Enterogastrone inhibits this action. The pancreatic enzymes are a single lipase, alpha and beta amylase, trypsin, chymotrypsin, a peptidase, a collagenese. Exclusion of the pancreatic juice causes changes of the lipid metabolism attributed to "lipocaic" deficiency but more likely due to a deficiency of choline.

The weakness of the provocative tests is their dependence on the degree of ductal obstruction on one hand and the parenchymal damage on the other, two factors opposing each other. The most reliable of these tests is the secretin test. This test may be normal in acute pancreatitis and is used only in chronic disorders. Pancreatic duct obstruction is shown by a reduction of fluid volume, parenchymal damage by a decrease of bicarbonate and enzymes. The choleretic properties of secretin makes it possible to check for abnormalities of bile flow at the same time and localize lesions of the hepatic, pancreatic and common ducts more properly.

H. B. EISENSTADT

TOTAL PANCREATECTOMY: Ichio Honjo. J. Internat. Coll. Surgeons 25:551 (May), 1956.

Total pancreatectomy should be accompanied by duodenectomy, cholecystectomy and anastomosis of the common bile duct into the jejunum.

Experimentally in dogs this procedure results in a markedly disturbed digestion and absorption of fats, proteins and carbohydrate. In man, however, the derangement is not so severe, 75 per cent of protein being digested and absorbed, 57 per cent of the fat and practically all of the carbohydrate, indicating a higher specialization of the human gastrointestinal tract.

Total pancreatectomy is a serious operation and these complications must be borne in mind, 1. development of ulcer at the site of gastrojejunal junction, 2. ascending infection in the biliary tract following implantation of the duct into the jejunum, 3. derangement of calcium metabolism, with a lakeing of this mineral from the skeletal system, 4. decreased function of the anterior portion of the pituitary gland, (although this prevents, in an unexplained manner, development of insulin resistant, postoperative diabetes), 5. hypoglycemia, under insulin medication, 6. fatty liver, despite correct insulin therapy.

One, 5 and 6 can be prevented by allowing the blood sugar level to remain at all times above the considered normal.

J. Edward Brown

PATHOLOGY AND LABORATORY RESEARCH

THE INFLUENCE OF THE AUTONOMIC DRUGS ON LIVER FUNCTION, PARTICULARLY ON THE METABOLISM OF UROBILINOGEN: Yuzo Shibata and Masatoshi Ikuno. Kyushu J. Med. Sc. 6:129 (Sept.), 1955.

The authors state that urobilinogen exists in a direct and indirect form corresponding to the direct and indirect forms of bilirubin. Urobilinogen absorbed from the intestines through the portal system is acted on by the parenchymal cells of the liver and then is further acted on by the reticuloendothelial system of the liver. In experiments conducted on rabbits the urine was tested quantitatively for these forms of urobilinogen after stimulation of the parasympathetics by pilocarpine; inhibition of the parasympathetics by atropine; and stimulation of the sympathetics by adrenalin.

The direct form was increased after excitation of the parasympathetics (pilocarpine) and reduced after paralyzing the parasympathetics (atropine) or stimulating the sympathetics (adrenalin). This increase the authors attributed to a decrease in the function of the reticuloendothelial system of the liver when the parasympathetic is stimulated; and its decrease after paralyzing the parasympathetics or exciting the sympathetics to an increase in the functional capacity of the reticuloendothelial system.

Samuel L. Immerman

THE INFLUENCE OF THE AUTONOMIC DRUGS ON THE QUANTITATIVE VALUE OF BILIRUBIN IN BLOOD: Yuzo Shibata and Eiichi Tabata. Kyushu J. Med. Sc. 6:133 (Sept.), 1955.

Continuing their experiments on the action of autonomic drugs on the quantity of excretion of urobilinogen in the urine, the authors also tested the effects of these drugs on blood bilirubin.

The authors had noted clinically that in the very early stage of catarrhal jaundice (infectious hepatitis) that bilirubin in the urine was markedly reduced after the administration of atropine. They had previously shown that urobilinogen of the urine was reduced in normal rabbits after the administration of atropine, and increased after pilocarpine.

The following experiments were performed: in normal rabbits a parasympathetic stimulant, pilocarpine, increased the value of the indirect form of blood bilirubin. Prostigmine had a similar effect.

Atropine (parasympathetic paralyzing drug) and Scopalomine were used in 12 normal individuals. The indirect form of bilirubin was decreased under the influence of these drugs.

Adrenalin (sympathetic stimulant), in 12 normal rabbits caused a decrease of indirect blood bilirubin.

The value of the direct form of bilirubin, regarded as having been regurgitated from the liver into the blood, was reduced after atropine. It will be noted that in normals it was the indirect form which was reduced.

In normals the indirect form of bilirubin predominates in the blood. The authors assume that as long as the liver function is normal it is the indirect form which is absorbed from the liver into the blood. In catarrhal jaundice the direct form of bilirubin is absorbed into the blood, but is not properly disposed of. Stimulation of the sympathetic nervous system (or paralysis of the parasympathetics by atropine) enhances the power of the disposal by the reticuloendothelial system and temporarily decreases the value of direct blood bilirubin in catarrhal jaundice.

SAMUEL L. IMMERMAN

STUDIES ON THE SPECIFIC ANTIGENS OF HUMAN GASTRIC CANCER, I: Katsutaro Kobayaski. Tohoku J. Exper. Med. 63:185 (25 Feb.), 1956.

Hirszfeld, Witebsky, Lehmann-Facious, and others found that there exist antigens specific to cancer in the alcoholic extract of human cancers. The author studied the phospholipid fraction of the alcoholic extract, a fraction soluble in benzene and insoluble in acetone and soluble in petroleum ether. His experiments were performed on human gastric cancer.

He prepared rabbit sera against alcoholic extracts of fresh human gastric cancer and fresh normal gastric mucosa and, aided by absorption tests, performed complement-fixation tests of these two antisera.

Complement-fixation tests were made against human gastric cancer and human normal gastric mucosa with alcoholic extracts of gastric cancer, normal gastric mucosa, and placenta. All the three extracts showed fairly intense reactions, whereas the extract of placenta did not react with the serum against normal gastric mucosa, differing from the other two extracts. This indicates that some antigens were common to both tissues: gastric cancer and placenta. By the use of gastric cancer serum, absorbed with 10 mg. of the placenta extract per 1 c.c., the antiserum reacted both with the alcoholic extract of gastric cancer and with the extract of normal gastric mucosa. When 8 mg. of extract of normal gastric mucosa per 1 c.c. of the serum was used, the antiserum reacted only with the extract of gastric cancer. This demonstrated there are specific antigens in the alcoholic extract of human cancer.

I. H. EINSEL

STUDIES ON THE SPECIFIC ANTIGENS OF HUMAN GASTRIC CANCER, II: Katsutaro Kobayaski. Tohoku J. Exp. Med. 63:191 (25 Feb.), 1956.

In the first paper, Katsutaro Kobayaski demonstrated specific antigens in the alcoholic extract of human gastric cancer. In these experiments he attempts to fractionate the alcoholic extract into different fractions. The material was prepared, exactly as in the first paper, from fresh material. The alcoholic extracts of gastric cancer and normal mucosa were fractionated with organic solvents. By referring to the results of the complement fixation test with each fraction as antigen, the fractionation was made finer and finer until the fraction responsible for the specific antigenicity of gastric cancer could give a single peak in an electrophoretic pattern when submitted to electrophoresis by the Tiselius method.

The material finally used was examined by qualitative analyses tests as substance *a* of gastric cancer and substance *a'* of normal gastric mucosa. Each presented an electrophoretic pattern bearing a single peak; each substance should be regarded as a single substance, not a mixture of two or more substances. Qualitative analyses of these substances gave the results: phosphorus test, ++; Molish's test, +; Elson-Morgan's test, +550.

Two substances specific to human gastric cancer were isolated. They are closely related. Each substance is a single one, presumably consisting of phospholipid and glycolipid.

I. H. EINSEL

BOOK REVIEWS FOR GASTROENTEROLOGISTS

PRACTICAL DIAGNOSIS AND TREATMENT OF LIVER DISEASE: Carroll Maton Leevy, M.D. Foreword by Franklin M. Hanger, M.D. 336 pages, illustrated in black and white and color. Paul B. Hoeber, Inc., New York, N. Y., 1957. Price $8.50.

This monograph represents years of painstaking study of liver diseases and embodies the author's observation of 1,000 patients with various diseases of the liver.

In the brief preface, Dr. Hanger summarizes the purpose of this book and the difficulty of selecting suitable material for inclusion.

The reviewer, who has written several texts on the liver, gallbladder and bile ducts, is extremely interested in Dr. Leevy's keen insight and profound knowledge pertaining to the diagnosis and treatment of hepatic disease.

Among the more recent monographs on the liver, this one far surpasses all others and is highly recommended as a valuable addition to the physician's library.

HISTAMINE—CIBA FOUNDATION SYMPOSIUM JOINTLY WITH THE BRITISH PHARMACOLOGICAL SOCIETY: G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch. and Cecilia M. O'Connor, B.Sc., Editors for the Ciba Foundation. 472 pages, 133 illustrations. Little Brown & Co., Boston, Mass., 1956. Price $9.00.

This entire volume is devoted to histamine and the various papers and discussions deal with its wide distribution in the various organs and tissues, including the skin, muscles, blood, plasma, bile, gastric juice and urine. It is also found in various plants and vegetables.

Physiologists, biochemists and research workers will greatly benefit from reading this monograph.

THE DOCTORS: Andre Soubiran. 380 pages, complete and unabridged, paper covers. Originally published by G. P. Putnam's Sons, Popular Library, Inc., New York, N. Y., 1956. Price $.50.

A vivid narrative dealing with Parisian medical students, their lives, loves and struggles. It is, however, an interesting description of the intrigues among the professors, their assistants, interns and nurses.

In some places, it is rather morbid and the book should not fall into the hands of teenagers.

LIVER, PANCREAS AND THE PORTAL SYSTEM: P. Mallet-Guy, J. Feroldi, Ch. Debray, M. Roux, A. Lemaire, L. Leger, J. R. Sicot and E. Housset. 141 pages, illustrated. Masson & Cie, Paris, France, 1956. Price 1,000 fr.

This book is made up of conferences held at the faculty of medicine in Paris by well known clinicians. These conferences deal with a complete review of the biliary system and the pancreas.

The bibliographies, with few exceptions, are all from French medical literature and several illustrations in black and white enhance the text.

THE PATHOLOGY OF THE PANCREAS IN CHILDREN: Dozent Dr. Med. Gerhard Seifert, Prosector am Pathologischen Universitats, Institut, Leipzig. 151 pages, 109 illustrations. VEB Georg Thieme, Leipzig, Germany, 1956. Price 52 DM.

An unusually well written, illustrated monograph on "The Pathology of the Pancreas in Children". There is an extensive bibliography, authors' and cross index. The bibliography covers the world's medical literature dealing with the pancreas. Embryology, physiology, abnormal states and diseases of this organ, leave nothing to the imagination. Translation into other languages would make this book a valuable addition to the physician's library.

J.A.M.A.—QUERIES AND MINOR NOTES: Published for the American Medical Association. 354 pages. The C. V. Mosby Co., St. Louis, Mo., 1955. Price $5.50.

Those of us who read the A.M.A. journal for years, usually after scanning the index on the front page, turn to the section on Queries and Minor Notes. The questions and scholarly answers help many physicians in their daily practice.

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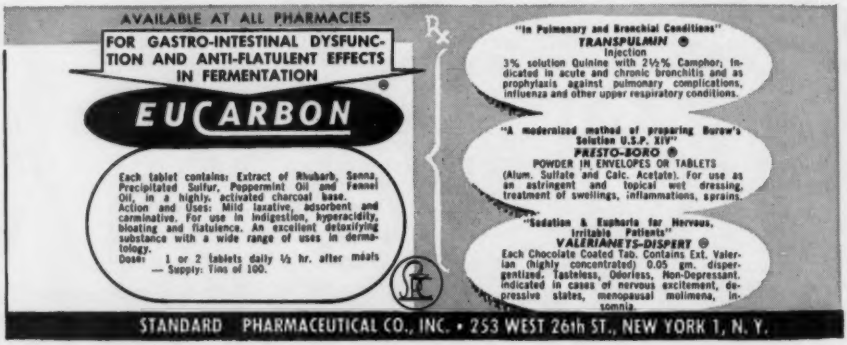

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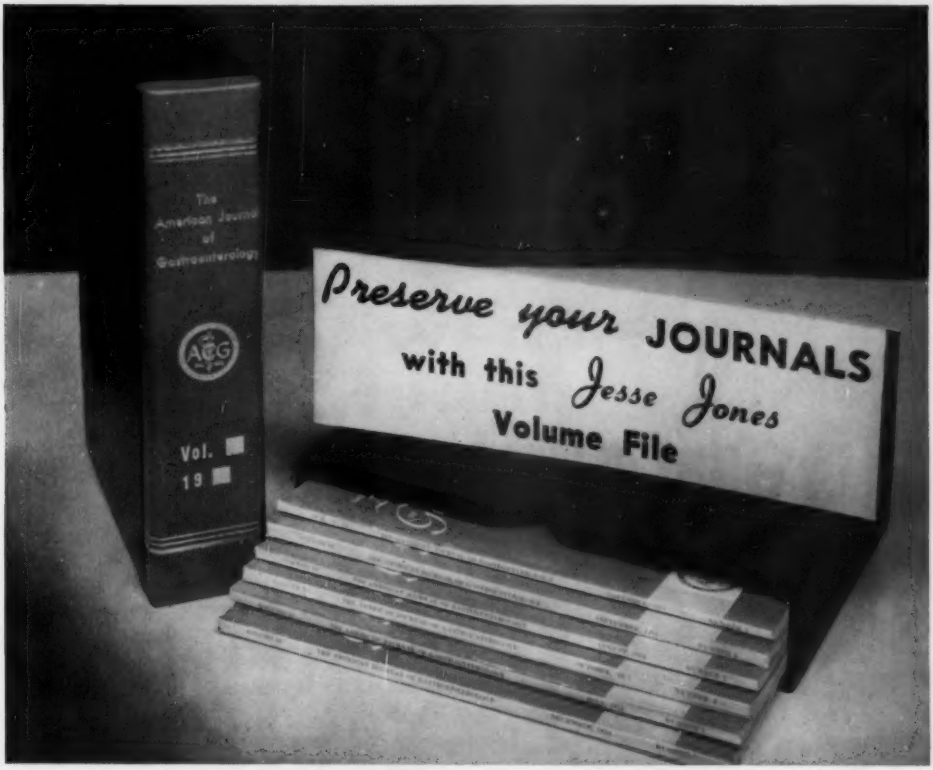

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1. Breidenbach, L., and Secor, S. M.: Proper Handling of the Colostomy Patient, Amer. J. Surg. 93:50, 1957.

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Confronting him, the tattered young man in blackface disguise saw the firegleam on his white silk shirt and pearl handled pistol and knew this was the murderous chieftain, Charlemagne Masena Peralte. The man he'd come for, through a jungle and a 1200-man encampment, past six hostile outposts, risking detection and certain death.

Charlemagne squinted across the fire. "Who is it?" he challenged in Creole.

There was no alternative; Marine Sergeant Herman Hanneken drew an automatic and fired.

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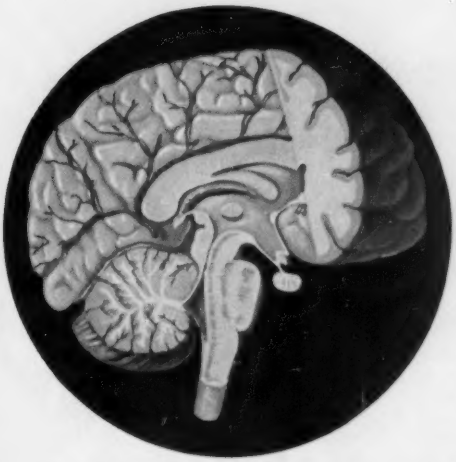

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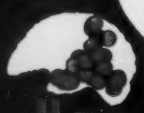
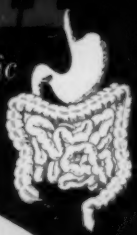
CM-5109

now "*. . . care of the man rather than merely his stomach.*"[1]



"Milpath"

Miltown® + *anticholinergic*



controls

gastrointestinal dysfunction

at cerebral *and* peripheral levels

tranquilization without barbiturate loginess

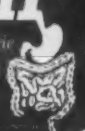
spasmolysis without belladonna-like side effects

for *duodenal ulcer • gastric ulcer • intestinal colic spastic and irritable colon • ileitis • esophageal spasm G. I. symptoms of anxiety states*

prescribe: 1 tablet t.i.d. at mealtime and 2 at bedtime.

"Milpath"

Miltown® + *anticholinergic*



Formula:

Miltown® (meprobamate) 400 mg. (2-methyl-2-n-propyl-1, 3-propanediol dicarbamate) U. S. Patent 2,724,720

tridihexethyl iodide 25 mg. (3-diethylamino-1-cyclohexyl-1-phenyl-1-propanol-ethiodide)

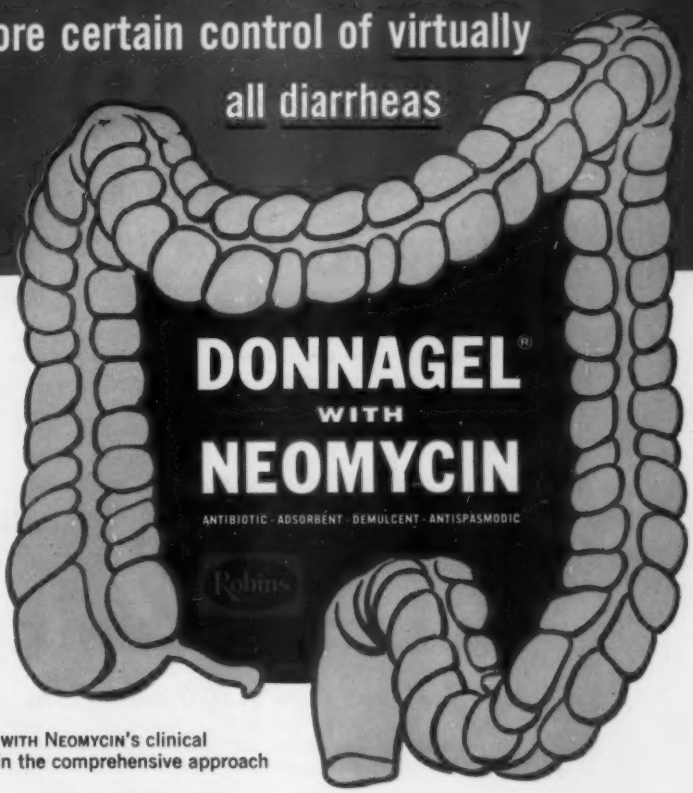
1. *Wolf & Wolff, Human Gastric Function*

Literature, samples, and personally imprinted peptic ulcer diet booklets on request.

WALLACE LABORATORIES New Brunswick, N. J.

– the preparation you've asked for

ANNOUNCING: a NEW antidiarrheal for more certain control of virtually all diarrheas



Addition of neomycin to the effective DONNAGEL formula assures even more certain control of most of the common forms of diarrhea. Neomycin is an ideal antibiotic for enteric use: it is effectively bacteriostatic against neomycin-susceptible pathogens; and it is relatively non-absorbable.

The secret of DONNAGEL WITH NEOMYCIN's clinical dependability lies in the comprehensive approach of its rational formula:

COMPONENT in each 30 cc. (1 fl. oz.)	ACTION	BENEFIT
Neomycin base (210.0 mg.) (as neomycin sulfate U.S.P.)	antibiotic	Affords effective intestinal bacteriostasis.
Kaolin (90 gr.)	adsorbent, demulcent	Binds toxic and irritating substances. Provides protective coating for irritated intestinal mucosa.
Pectin (2 gr.)	protective, demulcent	Supplements action of kaolin as an intestinal detoxifying and demulcent agent.
Dihydroxyaluminum aminoacetate (0.25 Gm.)	antacid, demulcent	Enhances demulcent and detoxifying action of the kaolin-pectin suspension.
Natural belladonna alkaloids: hyoscyamine sulfate (0.1037 mg.) atropine sulfate (0.0194 mg.) hyoscine hydrobromide (0.0065 mg.)	antispasmodic	Relieves intestinal hypermotility and hypertonicity.
Phenobarbital (¼ gr.)	sedative	Diminishes nervousness, stress and apprehension.

Robins

Informational literature available upon request.

INDICATIONS: DONNAGEL WITH NEOMYCIN is specifically indicated in diarrheas or dysentery caused by neomycin-susceptible organisms; in diarrheas not yet proven to be of bacterial origin, prior to definitive diagnosis. Also useful in enteritis, even though diarrhea may not be present.
SUPPLIED: Bottles of 6 fl. oz. At all prescription pharmacies.

DOSAGE: **Adults:** 1 to 2 tablespoonfuls (15 to 30 cc.) every 4 hours. **Children over 1 year:** 1 to 2 teaspoonfuls every 4 hours. **Children under 1 year:** ½ to 1 teaspoonful every 4 hours.
ALSO AVAILABLE: DONNAGEL, the original formula, for use when an antibiotic is not indicated.

A. H. ROBINS CO., INC., RICHMOND 20, VA.

anatomically correct rectal tube minimizes injury hazard

When administering an enema, it is unnecessary to force fluid high into the rectum. Instilled just beyond the internal anal sphincter, an enema induces increased pressure, resulting in colonic peristalsis.

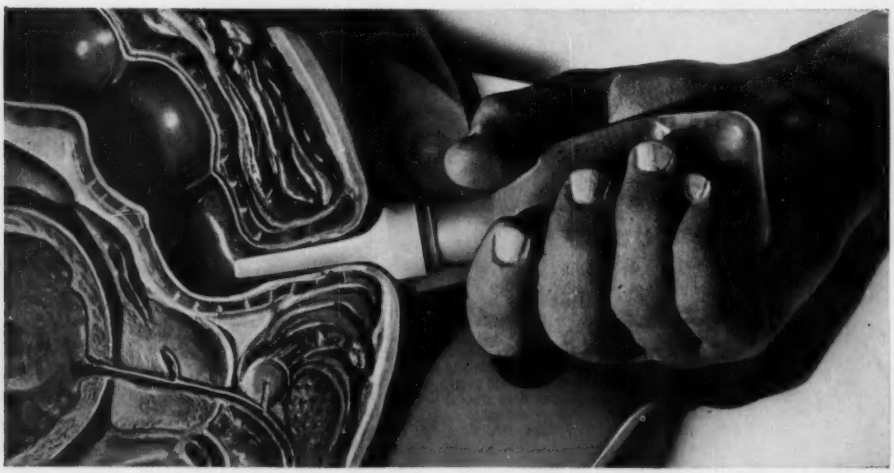
The pre-lubricated rectal tube of the FLEET ENEMA Disposable Unit is of anatomically correct design to deliver fluid most effectively while minimizing injury hazard . . . another reason why FLEET is rapidly becoming a Disposable Unit of choice whenever an enema is indicated.

FLEET® ENEMA

Disposable Unit

contains per 100 cc. 16 Gm. Sodium Biphosphate and 6 Gm. Sodium Phosphate . . . an enema solution of Phospho-Soda (Fleet).

C. B. FLEET CO., INC. Lynchburg, Virginia

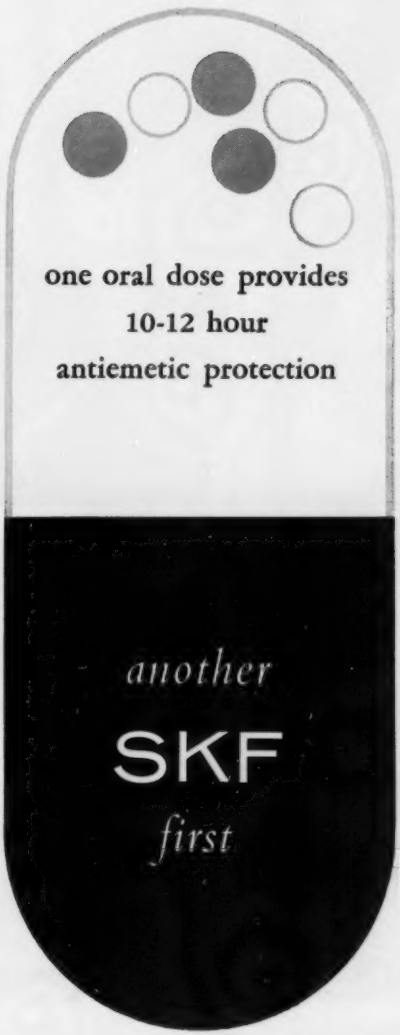


NEW

*Compazine** *Spansule*†

capsules

combine the advantages of the superior antiemetic and the unique sustained release dosage form



for prompt and prolonged control of the nausea and vomiting caused by:

pregnancy
viral gastroenteritis
terminal cancer
duodenal ulcer
postoperative conditions
radiation therapy
nitrogen mustards
migraine headaches
tension headaches
meningeal inflammation
psychogenic factors

Available: 10 mg. and 15 mg. 'Compazine' *Spansule* capsules

Smith, Kline & French Laboratories, Philadelphia

*T.M. Reg. U.S. Pat. Off. for prochlorperazine, S.K.F.

†T.M. Reg. U.S. Pat. Off. for sustained release capsules, S.K.F.

Patent Applied For.

NEW SIGNEMYCIN* V

advance in potentiated multi-spectrum therapy—higher, faster levels of antibiotic activity

OLEANDOMYCIN TETRACYCLINE-PHOSPHATE BUFFERED

Signemycin V—the new name for multi-spectrum Sigmamycin —now buffered for higher antibiotic serum levels.

capsules

New added certainty in antibiotic therapy —particularly for that 90% of the patient population treated at home or office where susceptibility testing may not be practical.

Signemycin V Capsules provide the unsurpassed antimicrobial spectrum of tetracycline extended and potentiated to include even those strains of staphylococci and certain other pathogens resistant to other antibiotics. The addition of the buffering agent affords higher, faster antibiotic blood levels following oral administration.

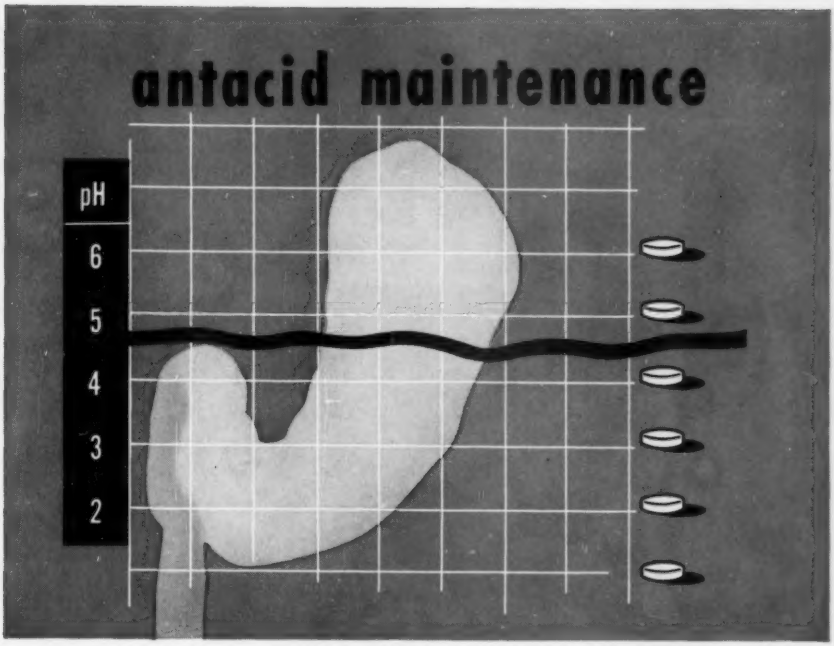
Supplied: Capsules containing 250 mg. (oleandomycin 83 mg., tetracycline 167 mg.), phosphate buffered. Bottles of 16 and 100.

*Trademark

World leader in antibiotic development and production

Pfizer

PFIZER LABORATORIES, Brooklyn 6, N.Y.
Division, Chas. Pfizer & Co., Inc.



Healing of peptic ulcer must be followed by effective antacid maintenance therapy to prevent recurrence. This can be achieved conveniently with agreeable, easy-to-carry Creamalin Tablets and Capsules.

Through sustained reduction of gastric acidity without the danger of alkalosis, nonabsorbable Creamalin provides reliable and safe antacid control for the ambulatory ulcer patient.

REACTIVE ALUMINUM HYDROXIDE GEL

Creamalin®

TABLETS: Bottles of 50 and 200
CAPSULES: Bottles of 100
LIQUID: Bottles of 8 and 16 fl. oz.

Winthrop LABORATORIES
NEW YORK 18, N.Y. • WINDSOR, ONT.

CREAMALIN, trademark reg. U. S. Pat. Off.

Division, Chas. Pfizer & Co., Inc.

put a new ending on this old tale

Old King Hal has many modern counterparts: executives who entertain . . . husbands who like "good eating," wives who serve "something different" . . . children who like "gooey" sweets. But for each the aftermath is often uncomfortable.

With Gelusil tablets or liquid, however, you quickly, soothingly relieve acute and chronic excessive gastric acidity! And Gelusil helps you manage the gnawing pain of peptic ulcer, too.

Gelusil stabilizes burning gastric acid within normal pH range, usually in minutes.

- *Gelusil works fast*
- *Gelusil is long-lasting*
- *Gelusil won't constipate*

Your patients get nightlong, sleep-assured protection with new formula Gelusil-Lac. By combining Gelusil's proven antacid action with the buffering effect of high-protein, low-fat milk solids, Gelusil-Lac *prevents* "middle-of-the-night" gastric pain!

there's no laxative in Gelusil . . . Gelusil needs no laxative

Gelusil®/Gelusil-Lac

WARNER-CHILCOTT

100 YEARS OF SERVICE TO THE MEDICAL PROFESSION